

BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 36, No. 7

July, 1961

Public Health

The order in this section is:—General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.

GENERAL

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE.

The Report of the United States Public Health Mission to the Union of Soviet Socialist Republics including Impressions of Medicine and Public Health in Several Soviet Republics, August 13 to September 14, 1957. *Pub. Health Service Publication No. 649.* pp. vi + 67, illustrated. 1959. Wash. 25, D.C. Superintendent of Documents, U.S. Govt. Printing Office. [\$0.45.]

This is an interesting report on the 4 weeks' visit of this United States Public Health Mission to the Union of Soviet Socialist Republics in 1957 which may be studied in conjunction with other published accounts on Russian medical activities [see this *Bulletin*, 1956, v. 31, 881; 1959, v. 34, 974; 1960, v. 35, 529].

In the introduction there is some description of the geography, climate, demography and political and civil organization of the Soviet Union. This is followed by sections on the organization, structure and philosophy of health and medical services; medical and related education and on medical scientific research. There are appendices on the "Problem Plan of the Academy of Medical Sciences of the U.S.S.R. for 1956-60" and on the many pamphlets and articles which were presented to the Mission. A considerable number of photographs, charts, maps and tables are included in the report.

Tribute is paid to the hospitable and helpful attitude of the Russians who had prepared the extensive itinerary with care and provided much information although some facts and figures were "deliberately withheld".

In the preface great credit is given to the medical achievements for "Although the present standards of quality of medical care and medical education in the Soviet Union fall far short of those in the United States" nevertheless "One of the dramatic accomplishments in health in recent times has been the almost explosive extension of disease prevention and medical care over the vast extent of the Soviet Union." The health picture has been changed, the "surging epidemics" of the past are stated to have disappeared, malaria is no longer a significant problem, "venereal disease has been mastered" although "tuberculosis remains a plague".

(L.331)

In the conclusions the medical activities of the U.S.S.R. are compared with those of the United States. In Soviet society the physician is "less accepted as a builder of the national health than as a special technician who may help or salvage useful manpower". He is not allowed the higher priority assigned to "citizens who contribute most to the security, solvency, economic growth, and prosperity of the State". There are many other differences such as that the Soviet system does not allow free choice of physician or permit the physician to select his place of practice.

M. E. Delafield

CALIFORNIA, STATE OF: **Health Care for California. A Report of the Governor's Committee on Medical Aid and Health** [EGEBERG, R. O., Chairman]. pp. v + 104, illustrated. [Numerous refs.] 1960, Dec. Berkeley 4: Dept. of Public Health, 2151, Berkeley Way, California, U.S.A.

This is the report of a Committee set up by the Governor of California in December, 1959 with the charge to: "1. Study broadly the health needs of citizens; 2. Investigate present provision for, and the cost of, health services; 3. Outline a long-range health program and its support; 4. Recommend immediate and specific action to assure a high standard of medical and health care for all Californians."

In a short introduction there is a sketch of modern conditions and problems of health and medical care with emphasis on the vast additions to medical knowledge which have brought about a great increase in the cost of medical care and the need for specialization and "sub-specialization". The Committee also stress that their recommendations in respect of planning for the future are, on the whole, aimed at decentralization.

A chapter on population and health contains a short account of the increase in population in California where migration adds more to the numbers than does natural increase. The State enjoys a high educational level and a high *per caput* income. Infant, maternal and total death rates are lower than in the country as a whole but there are problems of chronic disease of ageing, of the

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higher mortality of non-whites than of whites, which are among other problems to be tackled.

Succeeding chapters are on the organization and distribution of health services; paying for personal health services; hospitals; health manpower; the spectrum of health services; prevention of illness; diagnosis and treatment; rehabilitation; population groups with special health problems and summary of conclusions and recommendation. All these subjects were considered in very great detail and their descriptions together with the conclusions and recommendations of the Committee are set out fully and clearly.

Much attention is given to the subject of cost. In the chapter on paying for personal health services it is stated that the rising costs of health care have become burdensome to many, in particular the low income

groups, the aged, the chronically ill, and the disabled. Although ever larger sums for health services are being paid by the people of California yet not enough is spent to provide for comprehensive services such as prevention, organized home care and rehabilitation. "The Committee believes that the most practical way to meet the cost of personal health care is through prepayment, the enormous potential of which has been amply demonstrated in the past 15 years." It is also stated "The people of California now spend more than two billion dollars a year for health services. About three-fourths of this total flows through private channels, including a substantial proportion through voluntary prepayment plans. About one-fourth is spent by governments." In addition there is the cost of hospital facilities and the training of medical personnel.

M. E. Delafield

VITAL STATISTICS

HUNT, Eleanor P. & CHENOWETH, Alice D. **Recent Trends in Infant Mortality in the United States.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 190-207, 2 figs. [26 refs.]

The downward trend of the infant mortality in the United States was interrupted in 1957 by a slight rise. The infant mortality rose by 0.3 to 26.3 per 1,000 live births, the rise for white infants was 0.1 and for the non-white infants it was 1.6. For both white and non-white infants the metropolitan rate increased more than the non-metropolitan rate. Among the white infants the neonatal rate remained unchanged at 17.5 per 1,000 live births and the post-natal rate rose 0.1 to 5.8. The neonatal mortality of the non-white infants rose by 0.8 to 27.8 and the post-natal rate, 15.9, also showed a rise of 0.8. Considerable variations existed in the size of the rate between States, from 21.2 per 1,000 live births in Utah and Iowa to 35.6 in Arizona. During recent years the infant mortality of the States with the lowest rates has undergone very little change while the States with the highest rates have shown the largest actual and relative falls.

W. J. Martin

to 1,842 has occurred among the non-white births. There has been a steady rise in the proportion of births without prenatal care, for those born in the city hospital the rise has been from 30% in 1952 to 47% in 1957 and 1958.

The author concludes that the rise in the perinatal mortality was due to the fact that the changes in the population have produced a higher proportion in need of public services and that the services have not kept pace with the demand. Steps have been taken to remedy this defect.

W. J. Martin

HOOGENDOORN, D. Doodgeboorte en zuigelingensterfte van de onwettig geboren. [Stillbirths and Infant Mortality in Relation to Illegitimate Births] *Nederl. Tijdschr. v. Geneesk.* 1961, Feb. 25, v. 105, No. 8, 376-80, 4 figs. [10 refs.]

From 1840 to 1958 the illegitimate birth rate, in the Netherlands, had fallen from 5% to 1%.

To assess the influence of illegitimacy on mortality and stillbirths, figures covering 1953-1958 were analysed.

The major results were:—

	Legitimate	Illegitimate
Stillbirths	17/1000	20.5/1000
First born	31%	70%
Mothers over 35 years old	20.6%	10.7%
Infant mortality		
(covering 1957-58, 464,322		
legitimate and 5,829		
illegitimate live births)	17.1/1000	26.9/1000
Institutional confinement	25.9%	53.2%

Mortality amongst illegitimate infants is 71% higher in the first 3 days, 70% in the first week and 79% for the rest of the year, than in legitimate infants.

Examination of the causes of death showed high figures for infections (*i.e.*, respiratory and gastrointestinal diseases etc.), and in the "remaining" or miscellaneous group.

OPPENHEIMER, Ella. **Population Changes and Perinatal Mortality.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 208-16, 1 map & 9 figs.

A rise in the perinatal death rate (stillbirths and deaths in the first month of life) from 35.6 to 36.5 per 1,000 births in the metropolitan area of the District of Columbia was recorded in 1957. Since the end of the war there has been a large growth in the population, the proportion of white to non-white remained unchanged for the whole area but in the city area the white population has declined by 26% and the non-white has increased by 48%. The illegitimate births have risen from 1,935 in 1949 to 3,750 in 1958. The proportion of premature babies has decreased among the white infants but a rise from 1,255

Investigations on these lines can help materially to determine the aetiology in these, so frequently preventable, deaths.

Kurt Schwarz

BUETOW, Kathleen C. **An Epidemiological Approach to the Problem of Rising Neonatal Mortality in Baltimore.** *Amer. J. Pub. Health.* 1961, Feb., v. 51, No. 2, 217-27, 1 fig.

The neonatal mortality in Baltimore increased from 22 per 1,000 live births in 1956 to 26 in 1957. The rate for the white babies rose from 18 to 19 and the Negro rate rose from 27 to 36 per 1,000 live births. When it was found that the rise was persisting an investigation into the causes was carried out within two large hospitals. In hospital A, 85 of the patients were Negro and 40% of the Baltimore Negro babies were born in the hospital, in hospital B about 52% of the births were white. Factors which were correlated with the rise in neonatal mortality in hospital A were (a) the rise in the proportion of patients having no prenatal care (b) the increase in puerperal morbidity (c) changes in the age distribution; a larger proportion of babies became ill and died after the first 48 hours of life (d) excessive dosage of chloramphenicol in the newborn, particularly premature infants. These factors played no part in the rise in hospital B where the increase in the number of immature deliveries was sufficient to account for the slight rise in neonatal mortality.

W. J. Martin

GRIFFITHS, Joan. **The First Year of Life of the Johannesburg Bantu (1).** *South African Med. J.* 1960, Nov. 26, v. 34, No. 48, 1011-14, 1 fig. [11 refs.]

The author points out that the registration of births among the Bantu of Johannesburg is not accurate, though the position has greatly improved in recent years. Registration of infant deaths, on the other hand, is reliable because it is essential before burial can take place. Therefore, because formerly the births were underestimated, the infant mortality was overestimated, and the striking reduction from 411 per 1,000 live births in 1943-44 to 132 in 1958, shown in the available statistics, is an exaggeration. The Bantu rate now is similar to that for England and the United States at the beginning of the century and for American Negroes in the 1920s; it is much higher than the European (25), Coloured (63) and Asian (48) rates for Johannesburg.

The causes of death recorded for Bantu infants are largely diarrhoea, respiratory diseases, and diseases peculiar to the first year of life; infection and poor nutrition are more important than in the Europeans and Asians, and more deaths occur in later infancy than is the case with Europeans and Asians. Prematurity is an important factor, on the assumption that babies under 5½ lb. at birth are premature, as many Bantu babies are in this category.

The author concludes optimistically, for recent trends "offer great encouragement to those engaged in preven-

tive and curative medical work" among Johannesburg Africans.

Charles Wilcocks

TIMMER, M. **Child Mortality and Population Pressure in the D.I. Jogjakarta, Java, Indonesia. A Social-Medical Study.** [Thesis.] 501 pp., illustrated. [Numerous refs.] 1961. Amsterdam: University of Amsterdam.

The densely populated district of Jogjakarta is situated in the centre of the island of Java and consists of fertile valleys and uninhabited mountainous country. The district has the problem of an increasing population which has grown beyond the food resources of the country. This problem is similar to that in India, Pakistan, China, Egypt and many other parts of the world. The history of the area has been traced from the end of the 16th century and the customs and beliefs of the people which conflict with any changes in the living conditions are discussed. The estimated birth rate is 40 and the estimated crude death rate is 22 per 1,000 of the population and as a result of these rates the population is increasing rapidly. The pressure of the increasing population on the land has resulted in over-cropping and erosion and in some migration to the only large town in the area. The problem of food supplies becomes more intense every year and malnutrition is a very serious problem.

The infant mortality is estimated at 150-170 per 1,000 births and the death rate among toddlers was 43 per 1,000. The death rate among young children is discussed at length and the various hypotheses on which it is based are examined since there is no reliable registration on which to base rates. 1,300 children died in hospital during the 4 years July 1954-July 1958. Malnutrition was the most important cause of death up to age 4, accounting for 36.0% of all deaths at age 1, 40.1% at age 2 and then falling to 18.9% at age 5-6 years. Infectious diseases increase in importance with age, rising from 10.4% of all deaths at age 1 to 34.1% at ages 5-6 years. Prematurity and tetanus were the most important causes of death in the first month of life.

Malnutrition is an important cause of death in young children in Jogjakarta and the clinical picture is described in detail together with the type and length of treatment. The available foodstuffs with their calorie and protein values and the amount of the diet are given. The rapidly increasing population and the regular deterioration in the harvests is resulting in annual famines in the months of October-February. Modernization and mechanization in agricultural methods together with the necessary fertilizers and pest control would solve the immediate nutritional problem; but if the rapid rate of population increase remained unchanged starvation would reappear. The country lacks mineral resources so that it is unlikely that industrialization can play any very large part in the future life of the people. Severe handicaps in improving the standard of agriculture are the customs, beliefs and social structure of the community. The author discusses at length the social and economic implications of some of the suggested remedies and their impact on tradition,

and suggests that one essential is some form of family planning although this is resisted by the Muslims and Roman Catholics.

This extensive survey of the problem of subsistence

and a growing population in Java showed that the medical treatment of malnutrition is only a palliative measure and a more comprehensive approach to the problem must be employed.

W. J. Martin

EPIDEMIOLOGY

HARGREAVES, E. R. **Epidemiological Studies in Cornwall.** *Proc. Roy. Soc. Med.* 1961, Mar., v. 54, No. 3, 209-16 (Sect. Epidem. & Preventive Med. 1-8), 8 figs. [19 refs.]

Here presented are the results of epidemiological study of the incidence and distribution of disseminated sclerosis and of tuberculosis in Cornwall.

The introduction gives an account of some of the literature on the different hypotheses of the causation of disseminated sclerosis, its prevalence in different parts of the world and the experience of its mortality rates in England and Wales during the period 1921-58. Information on the disease in Cornwall during the last 20 years or so was obtained by search of the registers of death and from the Health Service and from general practitioners. In a 20-year period in an average total population of 332,943 there were 244 deaths from disseminated sclerosis or an average annual crude death rate per 100,000 of 3.67. The prevalence in 1958 was 214 persons with the disease in a population of 338,770. Maps of Cornwall give the mortality and prevalence rates by areas and these show that an area which includes Bodmin, Padstow and Wadebridge had the highest rates. An account is given of multiple cases—2 instances of both husband and wife being affected and a story of 4 "connected patients" in the same town.

In the section on tuberculosis in Cornwall there are several tables and figures to illustrate the trend of the disease. In the period 1948-59 the notifications were reduced by 62% in the 15-24 years age-group, to a satisfactory extent at 25-44 and 0-14 years but at over 45 years notifications in men increased by 105% and in

women by 30%. Tuberculin sensitivity rates on children comparing 1954-55 with 1959 indicate "that the amount of the active disease at large in the community has been greatly reduced, particularly in West Cornwall".

M. E. Delafield

GORDON, J. E., SINGH, S. & WYON, J. B. **A Field Study of Deaths and Causes of Deaths in Rural Populations of the Punjab, India.** *Amer. J. Med. Sci.* 1961, Mar., v. 241, No. 3, 359-82, 2 figs. [38 refs.]

This study covered 11 villages with a population of 12,000 observed for 4 years. There were no qualified physicians in any of the villages and the majority of the people who died were not attended by physicians. The deaths were reported by a local government official who allotted one third of the deaths to cough and fever and one third to fever and weakness. A staff physician visited the villages once a week and every death was investigated by him and the cause established from the available evidence. The cause was established with relative certainty in about 65%, there was some doubt in 29% and in 6% the cause was unknown. The most important causes of death were infections, the rates per 100,000 for these causes were, 187 for acute diarrhoeal diseases, 121 for pneumonia, 110 for tuberculosis and 91 for tetanus. The death rates for the other large causes of death were 80 for heart disease, 80 for birth injuries, etc., 77 for cancer, 72 for typhoid fever, 63 for accidents and 50 for measles. For the past 15 years the death rate in these villages has shown a downward trend.

W. J. Martin

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

LEMPERT, Susanne M. **The Stockport Survey of the Aged.** *Pub. Health.* 1960, July, v. 74, No. 10, 382-91.

It is no exaggeration to say that the care of the elderly represents the single greatest challenge in the field of social welfare in industrialized countries today. It is a challenge which can only be met by a common onslaught on the problems raised by all social welfare services including the health service. This account of the living conditions of 88% of those aged 80 and over in the

County Borough of Stockport underlines the closeness of the association between the social characteristics of the elderly and the problems of their social and medical care.

Marital status is an important factor in determining whether people over 80 can be cared for in their own homes or in the community. The never-married, followed by the widowed, are the most likely to need institutional care. They are also more likely to be found living on their own or with members of their own generation only. It was clearly people in these latter types of household,

too, that were most likely to have inadequate diets and to need hospital treatment.

Social status, measured according to the Registrar-General's Social Class classification, and economic factors were also related to type of household and to other aspects of medical and social care. A higher percentage of Social Class I and II were living with members of a younger generation than was the case in other social classes. Social Classes IV and V were more likely to be found both in institutions and living on their own. They were also more likely to be living in dwellings which lacked such amenities as a fixed bath, a piped hot water supply, an indoor lavatory and convenient coal storage facilities.

This valuable survey indicates that in Stockport the problems of maintaining mobility, preventing illness and

retaining independence in old age are, on the whole, more severe for those who lack spouses or younger relatives and for those who have never undertaken anything other than unskilled work. Those who are fortunate enough to have a living spouse and to be survived by offspring, as well as those who have sufficient means not to have to rely on National Assistance, are more likely to retain their independence to a ripe old age. The conclusions which emerge are, firstly, that social policies should be directed to promoting solutions which ensure reasonable economic security in old age and the provision of suitable housing for elderly people attached or near to their younger family's home. The author concludes: "The care of the aged can no longer be isolated from the rest of family care which is as much the aim of a public health service as it is the province of the general practitioner".

Margot Jeffreys

CHRONIC CARDIO-RESPIRATORY DISEASES

COOPER, ANN W., WILLIAMSON, G. M., ZINEMANN, K., EDWARDS, G. F. & THORTON, H. **Chronic Bronchitis. Changes in the Bacterial Flora of the Sputum associated with Exacerbations and Long-Term Antibacterial Treatment.** *Brit. J. Dis. Chest.* 1961, Jan., v. 55, No. 1, 23-9. [17 refs.]

The authors investigated the effect of oxytetracycline and triple sulphonamide on the viable count of *Haemophilus influenzae* and the pneumococcus in the sputum of patients with chronic bronchitis. They also sought to elucidate the association of these two important potential pathogens with winter exacerbations. The 24 patients chosen for this survey were known from a previous study to have *H. influenzae* "reasonably consistently" in their sputum. They were divided into two groups, the first being treated with 1 gm. oxytetracycline plus 1 gm. triple sulphonamide daily from October 1956 until April 1957, while the second group received dummy capsules. During the corresponding period in 1957-58 the groups were reversed. Of the 24 patients complete records were available for 9 only.

Despite careful examination the only potential pathogens consistently found were *H. influenzae* and the pneumococcus. In the majority of viable bacterial counts *H. influenzae* predominated. When the treatment and control groups were compared it was observed that there was a persistent, but not statistically significant, reduction in the numbers of viable *H. influenzae* per

ml. of sputum in the treatment group compared with the control group. A similar reduction was not seen when the pneumococcus was considered. Although the numbers per ml. of sputum of both *H. influenzae* and pneumococcus increased during exacerbations the increase was less marked in the treatment group than in the control group and this difference was due to the suppression of the *H. influenzae* rather than of the pneumococcus. These findings are quite different from those obtained by the British Tuberculosis Association [this *Bulletin*, 1960, v. 35, 421] which postulated that small doses of penicillin or oxytetracycline in chronic bronchitis shorten the length of exacerbations by virtue of the suppression of pneumococcus infections while *H. influenzae* remains uninfluenced. The ratio of time spent in bed, off work, or both, to the total duration of exacerbations was significantly less in the treatment group than in the control group and this result is in accordance with the findings of other workers.

Only two of 12 strains of *H. influenzae* examined showed a 5-fold increase of resistance to oxytetracycline after 6 months' continuous combined oxytetracycline-sulphonamide treatment, while the other 10 strains were as sensitive at the end of the 6-month period as at the beginning.

The authors indicate the need for further surveys of the type described, with a variety of antibacterial substances, but point out the various difficulties associated with such a task.

[See also this *Bulletin*, 1958, v. 33, 101 for an earlier study.]

Norma Temple

CANCER

LINELL, F. **Axplock ur en cancerstatistik. [A Sample of Cancer Statistics]** *Svenska Läkartidningen.* 1961, Feb. 24, v. 58, No. 8, 499-503, 2 figs.

Malmö has a population of 225,000 and is served by a general hospital at which post-mortem examinations are carried out on 99% of deaths which occur there.

Of the town's 1,797 deaths in 1959, 1,094 occurred in this hospital. These deaths, verified post mortem, are recorded graphically in a figure which shows that the stillbirths and deaths during the first year of life are prominent. After this age deaths are scarce up to the age of 35 when the death rate begins to rise slowly, with imposing figures after the age of 65. The peak is reached at the age 75-79 years. (Traffic deaths are not included here.)

Another figure deals with the 432 malignant tumours found in 1959 in 401 subjects examined post mortem. (The tumours outnumber the subjects because in a few cases two or more different types of malignant tumour were found in the same body). The tumours are recorded graphically according to their site and according to whether confirmation was obtained post mortem of the clinical diagnosis of malignant disease, or whether (53 cases) the clinicians suspected malignant disease, but were unable to locate its site or origin, or whether (93 cases) the clinicians had overlooked malignant disease, leaving pathologists to discover it at autopsy. Together these last two sections (146 of a total of 432 malignant tumours) inspire scepticism over the accuracy and reliability of ordinary death certificates as a guide to the causes of death. As the second figure shows, this source of error varies greatly with the site of the malignant disease. When the site is the colon or rectum the disease is often overlooked, and when it is the brain this mistake is the rule rather than the exception. But when the site of the disease is the breast the overlooked cases are very exceptional. Not shown in this figure is the statement in the text that in as many as 32 cases the pathologists failed to confirm post mortem the diagnoses of malignant disease made by clinicians, who were thus shown to have made mistakes in both ways with quite distressing frequency.

Claude Lillingston

MUIR, C. S. & KIRK, R. **Betel, Tobacco and Cancer of the Mouth.** *Brit. J. Cancer.* 1960, Dec., v. 14, No. 4, 597-608, 15 figs. on 3 pls. [Numerous refs.]

The geographical distribution of betel chewing and knowledge of the chemical and pharmacological contents of the quid are reviewed.

Opinions have differed as to whether the habit is related to the incidence of oral cancer, but this is probably due to the failure to note whether the quid contains tobacco. Recent studies [e.g., SANGHVI *et al.*, this *Bulletin*, 1955, v. 30, 686; SHANTA and KRISHNAMURTHI, *Brit. J. Cancer*, 1959, v. 13, 381] provide strong evidence that the habit is responsible for a large proportion of oral cancers when tobacco leaf is present in the quid.

An extract of a quid containing betel leaves, stone lime, betel nut, "gambir" and tobacco was obtained by means of a process resembling chewing and was painted on the ears of 12 Swiss mice. The mice were painted daily for 2 years. One squamous carcinoma appeared 8 months after painting stopped and in another mouse a basi-squamous carcinoma appeared 6 months after painting had stopped. All have now died. Painting of a second batch of 41 mice began in April 1958 and is still in progress. 10 mice have died; one squamous papilloma which appeared has been removed. Varying degrees of other epidermal and dermal changes, similar to those caused by carcinogenic cyclic hydrocarbons, have been seen in other mice.

It is possible that positive results have been obtained in these experiments, whereas other workers using tobacco extracts have obtained negative results, because the tobacco, or other factors in the quid, act as co-carcinogens.

Richard Doll

MISCELLANEOUS DISEASES

HENDERSON, P. **Prevalence of Defective Hearing among School Children.** *Med. Officer.* 1961, Mar. 30, v. 105, No. 13, 185-7.

In this account of the present prevalence of defective hearing among school children it is stated that in 1959 in England and Wales 14 out of every 1,000 children examined at periodic medical inspections (excluding children at independent schools) had defective hearing. This figure is based on the examination of about one-third of the total school population of about 7 million. In most instances however the hearing defect was found to be slight and sometimes temporary.

From 1925 to 1947 the number of children found to have defective hearing was about 5 per 1,000 but has since increased to the 1959 figure of 14.7 largely as the result of better methods of enquiry and their more extended use. Chronic ear discharge has diminished considerably but the number of children who are now kept under observation has increased 7-fold, owing to

more thorough enquiry into clinical histories and the greater use of electric auriscopes by school doctors.

The instruction of partially hearing children in ordinary schools by teachers of the deaf is a relatively recent development but there is as yet insufficient knowledge of the percentage of the school population which is in need of this help. Early diagnosis, auditory training, more efficient hearing aids and increasing experience have resulted in many children being treated as partially hearing who, not so long ago, would have been regarded as deaf. There are tables and a description which give the present picture in comparison with that of the past.

A section of the paper contains discussion of the problem of deaf children in the light of recent developments which have had the effect of emphasizing hearing rather than deafness and "hearing-mindedness as contrasted with seeing-mindedness".

Defective hearing in school children remains as an important problem, yet "the record of the past 10-20 years is one of achievement, and one that has promise for the future".

M. E. Delafield

Sanitation

The order in this section is:—General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

KENNER, B. A., CLARK, H. F. & KABLER, P. W. *Faecal Streptococci. I. Cultivation and Enumeration of Streptococci in Surface Waters. Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 15-20. [11 refs.]

A new medium for faecal streptococci is recommended as follows. Proteose peptone No. 3, 10 gm.; yeast extract, 10 gm.; sodium chloride, 5 gm.; sodium glycerophosphate, 10 gm.; maltose, 20 gm.; lactose, 1 gm.; sodium azide, 0.4 gm.; sodium carbonate, 0.636 gm.; brom-cresol purple, 0.015 gm.; distilled water, 1,000 ml. It may be used as described for multiple tube tests or for membrane filters with the addition of 1 ml. of 1% triphenyltetrazolium chloride (TTC) or as a solid medium with 2% agar and TTC.

Water samples were incubated on these media for 48 hours at 35°C. and compared with results by the DA-EVA procedure of LITSKY *et al.* [this *Bulletin*, 1953, v. 28, 1077].

All pink or red colonies were counted as streptococci and it was shown that *Streptococcus mitis*, *Strep. salivarius*, *Strep. bovis*, *Strep. equinus* and *Strep. faecalis* and all its varieties and biotypes gave typical growth. Some growth of *Pediococcus cerevisiae* and *Lactobacillus plantarum* occurred but they did not produce acid or pink colonies.

The authors interpreted all these streptococci as belonging to the faecal streptococcus group as they have all been isolated from human or animal faeces and domestic or slaughterhouse wastes. The new medium by all procedures yielded higher results on 25 surface water samples than were obtained by the DA-EVA procedure. The greater number of species able to grow on the new medium is suggested in order to account for differences in productivity.

E. Windle Taylor

WALDBOTT, G. L. "The Physiologic and Hygienic Aspects of the Absorption of Inorganic Fluorides". Comments on the Symposium. *Arch. Environment. Health.* Chicago. 1961, Feb., v. 2, No. 2, 155-67, 3 figs. [88 refs.]

In this paper there are valuable comments on the symposium on "The Physiologic and Hygienic Aspects of the Absorption of Inorganic Fluorides" which was published in April, 1960 [this *Bulletin*, 1960, v. 35, 748]. These comments are not intended to detract from the information given in the "Symposium" but to point out that some of the observations there presented are "at variance with those emanating from other sources" and that "the discrepancies revolve mainly around the interpretation of some of the findings".

"Three basic shortcomings in fluoride (F⁻) research should be noted at the outset:

"1. F⁻ intake into the system, its assimilation and excretion are subject to great variation between persons.

"2. In contrast to extensive biochemical advances in F⁻ research, relatively few clinical data are available on how F⁻ affects the human organism.

"3. F⁻, one of the most reactive of all elements, is found in many organs and tissues besides bones and teeth."

In the body of the paper the critical comments based on comparative analysis of the findings presented in the extensive literature are presented. There are 2 main sections both of which include tables and figures. The first section on "Inconsistencies in Data on F⁻ Metabolism" deals with the wide variations in the amounts of F⁻ which taken into the system from food and by inhalation are absorbed, stored and excreted. Section II on "The Effect of F⁻ Absorption on the Human Organism" contains discussion on (1) the difficulty in appraising the F⁻ effect on the health of man and animals, (2) the lack of correlation of biochemical with clinical data and (3) the storage of F⁻ in soft tissues about which our knowledge is inadequate and there is great difficulty in evaluating "how accumulation of F⁻ in soft tissues affects their function".

M. E. Delafield

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

MOORE, B. A Recent Bacteriological and Epidemiological Study of Sewage Contamination in British Coastal Bathing Waters. *J. & Proc. Inst. Sewage Purification.* 1961, Pt. 2, 133-40, 1 fig. Discussion 141-8, 1 fig.

This paper summarizes the findings of the research committee, set up in 1953 by the Public Health Laboratory Service, to investigate the risk of bathing on polluted beaches. The committee carried out extensive bacteriological, epidemiological and topographical studies

of 40 polluted beaches in Britain [see this *Bulletin*, 1960, v. 35, 634]. Their findings are briefly presented together with the following conclusions: (a) Only where pollution is so extreme as to be aesthetically revolting is there any risk to health. (b) That owing to the many varying factors no satisfactory bacteriological standard can be laid down for bathing beaches.

The conclusions have offended many people connected with the public health field and the paper presented at the Institute's Annual Conference evoked an excellent discussion.

A. James

KELLY, Sally & SANDERSON, W. W. **Density of Enteroviruses in Sewage.** *J. Water Pollution Control Fed.* 1960, Dec., v. 32, No. 12, 1269-73, 1 fig. [14 refs.]

This is another of the series of interesting papers emanating from the New York State Department of Health Laboratories in Albany about enteroviruses in

sewage. A quantitative estimation of enteroviruses in sewage swabs, MOORE [this *Bulletin*, 1949, v. 24, 187] was made by virus plaque enumeration using monkey kidney cultures overlaid with agar medium and incubated at 33°C. A few experiments were performed using the FL strain of human amnion cells but only insignificant differences were noted. In some experiments catch samples were used and these also gave similar results. All samples were treated as described previously [Kelly, *ibid.*, 1954, v. 29, 890], 14 different serological types of enterovirus were isolated. The concentration of viruses in samples varied with the time of year from less than 20 to 400 plaques per 100 ml. The highest concentrations occurred in the summer months but continued low levels of excretion occurred throughout the year. Raw sewage had higher concentrations of virus than treated sewage, especially with chlorination or activated sludge treatment. The concentration of enteroviruses found was similar to that described for salmonellae and other bacterial pathogens. It was much lower than faecal *coli* or coliphages.

A. J. Beale

HOUSING

LUNN, J. E. **A Study of Glasgow Families living on One-Apartment, Two-Apartment and Three-Apartment Tenement Houses.** *Scottish Med. J.* Glasgow. 1961, Mar., v. 6, No. 3, 125-9.

The author compares various social and economic characteristics of 369 randomly selected families who were re-housed from one- two- and three-roomed apartments in old Glasgow tenement buildings. The purpose of the study was to see whether there was any reason for granting any greater priority in re-housing to families occupying one-roomed apartments.

The study indicates that those living in one-roomed apartments were more overcrowded, particularly where sleeping arrangements were concerned. They were, on the whole, younger families with smaller incomes, and lower standards of house management. They were less likely to have luxury items like television. On the other hand, their health records as measured by hospital admissions were no worse than those of families in

larger apartments, and their more frequent attendances at doctors' surgeries could be attributed to the greater proportion of pregnant women among them.

After re-housing, most of the differences between families from one-, two- and three-roomed apartments disappeared. Income differences narrowed; but many more of those from one-roomed apartments undertook hire-purchase commitments, presumably (although the author does not say so) because they needed more household goods and equipment to furnish their homes. There was an overall improvement among all the families in the standard of house management, although a rather smaller proportion of the families from one-roomed apartments than from two- or three-roomed apartments were rated as good.

[This survey has only a limited interest for the public health administrator. It does indicate, however, that the majority of families from slum property and overcrowded conditions can be expected to maintain a good standard of house management after re-housing.]

Margot Jefferys

ATMOSPHERIC POLLUTION

INTERNAT. J. AIR POLLUTION. London. 1960, Oct., v. 3, Nos. 1/3, pp. iii + 200, numerous figs. [Numerous refs.] **Aerodynamic Capture of Particles.** *Proceedings of a Conference held at Leatherhead, Surrey, January 13-14, 1960* [Edited by E. G. RICHARDSON].

The emphasis of the papers read at this conference was on the physics and mathematics of the process of capture. The first Session was devoted to theoretical and fundamental aspects, the second to experimental application of capture techniques, and the third to capture of particles by raindrops.

NAT. SOC. FOR CLEAN AIR. **Proceedings of the 27th Annual Conference, Harrogate, 5th to 7th October, 1960.** 178 pp., numerous figs. 1961. London: Field House, Brems Buildings, E.C.4. [25s.]

SAWICKI, E., ELBERT, W. C., HAUSER, T. R., FOX, F. T. & STANLEY, T. W. **Benzo(a)pyrene Content of the Air of American Communities.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 443-51, 6 figs. [26 refs.]

Benzo(a)pyrene is of special interest as it is known to be carcinogenic to animals and is suspected of being carcinogenic to man. It is present in the air, and originates from the combustion of fuel. The authors of this paper have measured the concentration in air of this substance by analysing many samples collected from various parts of the United States. The results of two studies are given. In one, monthly mean values are reported throughout a year for 9 United States cities; in the other, single mean values are given for 6 24-hour samples collected every 2 weeks.

The samples for the measurement of benzpyrene were collected from the air by filtration and then extracted with benzene. The hydrocarbons in the extract were separated chromatographically and determined spectrophotometrically.

The results showed that urban areas contained higher concentrations of benzpyrene in the air and in the particulates than did non-urban areas. The concentrations in air were found to vary between 0.01 and 61 $\mu\text{gm. per } 1,000 \text{ m}^3$ air. The monthly results showed that the concentrations of benzpyrene in the airborne particles was highest during the winter and lowest during the summer. The authors suggest that the low summer levels could be attributed to decreased use of liquid and gaseous fuels and action of sunshine and oxidising atmospheres.

The concentration of benzpyrene in the benzene soluble fractions of the particulates was also measured. This varied between 0.00093 and 0.26%. The concentration of benzpyrene in the particulates varied between 0.00001 and 0.041%. The authors compare these latter figures with cigarette tar (0.00002 to 0.0001%) and calculate that the exposure of benzpyrene was 100 times greater for an urban dweller than for a non-urban one. They also state that exposure was greater for a non-smoker in many large American cities than for a pack-a-day smoker in a non-urban community. They also calculate that in many American cities the exposure to benzpyrene for the urban dweller who smokes a pack a day is double that of the non-smoking urban resident.

The paper is clearly set out and gives a number of graphs and tables of results. A comparison of benzpyrene concentrations in various parts of the world is also given. This paper is a highly valuable contribution to the study of benzpyrene concentrations in the air.

B. T. Commins

CHOLAK, J. & SCHAFER, L. J. **The Concentrations of Oxidant (Ozone) and Nitrogen Dioxide in the Air of Cincinnati, Ohio.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 452-8, 6 figs. [10 refs.]

In order to study fully the formation of smog by photochemical reactions it is necessary to measure concurrently the concentrations of oxides of nitrogen, ozone and hydrocarbons. The authors of this paper have measured oxidant (as ozone), nitrogen dioxide and nitric oxide in the air of Cincinnati, Ohio, and give a number of results of the measurements made at 3 sites in the area.

The oxidant was determined by measuring the amount of iodine liberated from buffered neutral potassium iodide when the air was passed through this reagent. Nitrogen dioxide was determined by measuring the colour produced when the air was passed through modified Griess reagent. Nitric oxide was determined separately by first passing the air through weak potassium permanganate and then through more Griess reagent.

The authors present graphically in their paper the frequencies of occurrence of certain oxidant and nitrogen dioxide concentrations. In general they found that the oxidant concentrations did not follow the nitrogen dioxide, and also hourly concentrations of oxidant, nitrogen dioxide and nitric oxide in excess of 10 parts per 100 million occurred less than 1% of the time. The authors suggested that high oxidant levels were produced when parcels of air had been allowed to react over long periods of time. They found in addition, more oxidant on calm, hot, sunny days.

Seasonal and monthly figures for oxidant and nitrogen dioxide are also given. Diurnal variations were studied and showed that oxidant levels were lowest during the night and highest between noon and 4 p.m. Peaks in nitrogen dioxide did not follow this pattern at all. Generally the lowest nitrogen dioxide figures were found when the oxidant was at its highest value.

This paper would be of great interest to many people interested in air pollution, particularly those interested in photochemical reactions in the air. B. T. Commins

MOORE, H., HELWIG, H. L. & GRAUL, R. J. **A Spectrophotometric Method for the Determination of Mercaptans in Air.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 466-70, 2 figs. [12 refs.]

The authors describe a spectrophotometric method for the estimation of microgramme quantities of mercaptan in air. They absorbed their mercaptans in 5% mercuric acetate and to this solution added N-N-dimethyl-p-phenylene diamine which formed a red complex, the intensity of which was measured colorimetrically. They found that hydrogen sulphide, sulphur dioxide and nitrogen dioxide did not interfere with the method at the concentrations usually encountered in air pollution and industrial hygiene studies. They found other mercaptans also produced a colour with the reagent.

No results of measurements made with this method are given in the paper. The original paper should be consulted if it is intended to use the method.

B. T. Commins

SCHERBERGER, R. F., MILLER, F. A. & FASSETT, D. W.
The Determination of n-Butylamine in Air.
Amer. Indust. Hyg. Ass. J. 1960, Dec., v. 21, No. 6,
471-4, 3 figs.

The authors describe a colorimetric method for the estimation of small quantities of butylamine vapour in air. They absorbed the butylamine in isopropyl alcohol

acidified with hydrochloric acid and to this solution added 5 ml. of pyridine and 2 ml. of ninhydrin reagent. The solution was then heated on a water bath to 85°C. for 7 minutes, cooled and read in a colorimeter. Other alkyl amines were also found to produce a colour.

No results of measurements made with this method are given. The original paper should be consulted for details of the method.
B. T. Commins

Occupational Hygiene

The order in this section is:—General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.

GENERAL

DELAUNAY, P. **The Economic and Social Background of Industrial Medicine in Madagascar.** *Internat. Labour Rev.* 1961, Feb., v. 83, No. 2, 107-35.

The author gives an account of Madagascar and its economic situation.

The following is the percentage distribution of occupational activities in the national economy (the calculation is only made for the private sector but the public sector is similar):

Agriculture, fishing, forestry, saw mills	...	30
Extractive industries	...	3
Manufacturing industries and workshops	...	12
Building and civil engineering	...	8
Commerce, banking and the professions	...	15
Transport and lighterage	...	7
Domestic service	...	25
Total	...	100

A more detailed description of the nature of the various local industries is given in the original.

The sources of health hazards differ widely, some of them being only indirectly connected with employment, namely migration, and changes in geographical and social environment, and others being inherent in the work itself, namely the working environment, occupational diseases and employment injuries. The author gives a lengthy account of the occupational hazards present in the Madagascar mines, factories and agriculture, although it is apparent that much of the account is based on subjective assessment rather than precise facts. There are, however, some statistical analyses of industrial accidents relating to causes by branch of activity and to severity according to period of incapacity. The percentage frequency of accidents in relation to the number of workers in each branch of activity for 1958 is given in the following table:

Manufacturing	...	...	...	...	4-77
Transport	...	...	...	...	3-37
Commerce	...	...	...	...	1-68
Public utilities	...	...	...	...	1-29
Building and civil engineering	...	...	...	...	1-24
Extractive industries	...	...	...	...	1-07
Domestic service	...	...	...	...	0-84
Agriculture	...	...	...	...	0-33
All activities	...	...	...	...	1-64

When compared with the total wage earning population (221,380) the total number of accidents (3,651) gives an over-all percentage rate of 1-64.

There is a most interesting description of the Medical Care Service which has been organized for the country as a whole and which includes an occupational health service. It is not possible to do justice to the description in an abstract and interested readers should refer to the original publication, which is in any case well worth reading *in toto*. The occupational health service includes individual and group factory medical services and medical care is provided by full-time industrial medical officers and by part-time government doctors. The following Standards have been laid down by the Labour Code of December 15, 1952:

- (1) For all wage earners:—
 - (a) a thorough medical examination at least once a year;
 - (b) first aid and transport at the employer's expense to the nearest medical post;
 - (c) maintenance of general health standards, particularly anti-malaria prophylaxis;
 - (d) enforcement of special health and safety measures respecting the occupation concerned;
 - (e) compensation for employment injury.
- (2) In establishments with 100 workers or more, a daily medical examination of all workers who report sick.

(3) For migrant workers, housing and in some cases food rations.

(4) For women and children, more frequent medical examinations and special forms of protection.

Detection, care and prevention are the concern of medical services the cost of which is borne entirely by employers. Employers who set up joint services can obtain loans not only to meet initial installation costs but also to improve the medical equipment and provide more comprehensive medical treatment than required by law. [In Britain the latter activity is delegated by our Government to the Nuffield Foundation, without whose assistance there would have been no experiments in group industrial medical services.]

P. J. R. Challen

BEDWELL, C. H. **The Problems associated with Fine and other Visually Difficult Concentrated Tasks in Industry.** *Ann. Occup. Hyg.* London. 1961, Feb., v. 3, No. 2, 84-93, 12 figs. (11 on 7 pls.)

This is an excellent scientific and technical paper on visual problems in industry.

"The problems associated with fine work have become more apparent in recent years because in some industries, for example electronics, there has been a strong tendency towards more and more miniaturization and finer limits. Yet because of normal competitive conditions the actual operation time must often be less than when the task was larger." The resulting visual difficulties and their practical solution are here discussed and described.

The main factors concerned in a seeing task are reviewed with references to relevant research under the headings: I. Task analysis—(1) size and visual acuity and (2) illumination, visual acuity and performance; II. The design of the visual field for efficiency and comfort—(1) lighting and colour and (2) the avoidance of glare; and III. The eyes at work—(1) eyestrain during concentrated vision, (2) the recording of eye movements, (3) prescribing for seeing of fine tasks and (4) the use of magnifying aids.

There are a number of very good photographs to illustrate the devices of lighting and magnification which are of value in different types of fine work and also of electro-oculograph and photographic equipment which has been developed for the scientific study of eye movements.

M. E. Delafield

BOWMAN, H. M. **Rocket Propellants. Safety and Industrial Health Aspects.** *Arch. Environment. Health.* Chicago. 1961, Mar., v. 2, No. 3, 293-306, 11 figs. [Numerous refs.]

The tremendous power of a rocket engine compared to its weight makes the rocket principle applicable to rock and oil well drilling as well as to airborne and military devices. Photographs add to the interest of the address to the Industrial Hygiene Foundation meeting at Pittsburgh in October 1960. Test areas were designed for thrust chambers of impulse ranges up to 1 million pounds thrust. In propellant research and development, safety training against hazards of detonation, fire, con-

tamination, corrosion and numerous troublesome and toxic chemicals starts with laboratory discipline. Bench, pilot and production stages bring additional considerations of atmospheric and countryside contamination from fumes and combustion products. Nevertheless the plant with 1,500 employees operated more than 300 days without a lost-time accident. Chemicals and safety measures are listed.

The most publicized fuels, the boranes, toxic to liver, kidney and lung, and which have caused reversible electroencephalographic changes, are worth while because of high heat of combustion and because boron is abundantly available. Some boron hydrides burn or explode if they leak from processing systems. Equipment made of metals except aluminium or magnesium is satisfactory; seals of most rubber and plastic materials and ordinary lubricants are not. Gasket materials include asbestos compositions, Teflon, Kel-F and metals.

Synthesis of new high energy molecules from micro quantities of chemicals is carried out in vacuum racks. Some materials are synthesized at ordinary, others at high atmospheric pressures. Fume-hoods may be standard, behind steel barricades or equipped with an air curtain. Curing is done in explosion-proof ovens enclosed in barricades. Soft-wall or blow-out panel construction or nitrogen blanketing also lessen explosive risks. Plexiglas shields have protected staff from fire and fragments. Articulated tongs are used. Analyses are carried out in inert atmosphere chambers, Parr bomb calorimeters, and Crawford Bomb Strand Burners, behind shields. [See also this *Bulletin*, 1960, v. 35, 440, 764.]

M. Patricia Fitzsimons

HÁJÍČKOVÁ, V. **Epidemie astmatu. [An Epidemic of Asthma]** *Časopis Lékařů Českých.* Prague. 1960, Nov. 25, v. 99, No. 48, 1511-14. [15 refs.] English summary.

The author describes an outbreak of asthma which occurred in 1950 among workers in a furniture factory in Czechoslovakia. 13 persons were affected among a total of 24, and 8 required treatment in hospital. The patients ascribed their symptoms to the use of a new type of cold glue. Skin tests carried out with the glue gave positive results in 22 persons; in 1 person scarification with glue diluted 1:100 evoked a severe attack of asthma with abdominal pains, nausea and diarrhoea, and another patient developed oedema of the whole arm which lasted several days. The attacks of asthma ceased when the use of the glue was discontinued and the type of production was changed.

D. J. Bauer

KAYE, M. & FREEDMAN, S. O. **Allergy to Raw Coffee—an Occupational Disease.** *Canadian Med. Ass. J.* 1961, Mar. 4, v. 84, No. 469-71.

Dust released when coffee beans were emptied from bags and the chaff separated caused eye, nose and chest complaints in a factory employing 400 workers. The bags were new and free from contamination from castor bean products reported in the literature to account for symptoms in coffee workers. Aqueous extracts

were prepared from chaff or beans, raw or roasted, to contain 1, 10, 100 or 1,000 protein nitrogen units per ml., and 0.4% phenol. Subjects selected for study were arbitrarily classified into 3 groups, 17 with no contact or symptoms, 39 considered allergic to coffee by the history and 56 with contact and no symptoms and not allergic by history. After intradermal injection of 0.025 ml. of an extract, any wheal was measured by graduated circles in a plastic ruler. The presence of pseudopods was considered a significantly positive reaction, and no more testing was carried out; in their absence all 16 extracts were tested.

No positive reactions occurred in the first group. Among the 39 composing Group 2, 27 were positive and of these 20 had a previous or a family history of allergic disease. There were 8 positive reactors among the 56 subjects in Group 3. Of 65 non-reactors, *i.e.*, Group 1 plus the remainder of Group 3, only 31 had past or family history of asthma, hay fever, etc.

The positive reactions were almost entirely limited to the raw extracts, particularly chaff extracts. However, extracts of raw beans from which the outer coat, possibly contaminated by chaff, was dissected, when tested by passive transfer against the serum of a positive reactor, again gave a positive reaction. Investigations are proceeding in order to lessen dust and to identify the antigen.

M. Patricia Fitzsimons

MINISTÈRE DE LA SANTÉ PUBLIQUE. Paris. Accidents du travail et facteur humain. Étude statistique. [Occupational Accidents and the Human Factor. Statistical Studies] [POULIZAC, H. G.]. *Monographie de l'Institut National d'Hygiène No. 21*. 196 pp., illustrated. [Numerous refs.] 1960. Paris (16e): Inst. Nat. Hyg. 3, rue Léon-Bonnat.

This monograph has been written by Dr. H. G. Poulizac, Medical Adviser to the Regional Office of the Sécurité Sociale at Nancy. The first half of the report is devoted to a detailed statistical analysis of occupational accidents in France in 1956 based on information supplied in a document published by the National Office of the Sécurité Sociale, entitled *Statistiques Nationales d'Accidents du Travail*. This information is classified under two main headings, *viz.* geographical, which is subdivided according to the areas of 16 regional offices, and occupational, which is subdivided according to 15 main professional groupings. The statistical analyses throw light on many aspects of the subject, for instance, frequency and severity rates, cost of accidents, the site of injury, the relative preponderance of temporary and permanent incapacity, the distribution of injuries according to age, sex and professional status and the incidence of various types of injury in different occupations and in different geographical areas.

In the second part of the report there is some very able discussion on the implications of the statistical study and on ways and means of improving the existing accident prevention and rehabilitation services. The discussion includes such subjects as the professional training of apprentices, physical training for adolescents and adults, the rehabilitation of injured persons, the provision of

suitable work for temporarily and permanently handicapped persons, social rehabilitation of the injured, and the provision of employment in sheltered workshops. Suggestions are put forward for the co-ordination on a regional basis of all the agencies concerned with the prevention of accidents and the treatment and rehabilitation of injured persons; regional centres would also engage in research activities.

This is an excellent monograph which merits close scrutiny by those interested in the subject for it contains a mass of facts, much learned reasoning, a practical programme for future development, and the whole is permeated by the basic philosophy that man and his environment should exist in a state of balanced equilibrium. Accidents are regarded as a manifestation of conflict between man and his background and of disturbance of this balance.

P. J. R. Challen

ROCHE, L., MAITREPIERRE, J., LEJEUNE, E. & MERMET, J. Les atteintes du membre supérieur chez les ouvriers travaillant au marteau pneumatique. [Upper Limb Damage in Pneumatic Drill Workers] *Arch. Malad. Professionnelles*. Paris. 1961, Jan.-Feb., v. 22, Nos. 1/2, 57-61.

The investigations described here were undertaken to study the frequency of the disabilities of the upper limb in miners which might be due to their work with pneumatic tools.

In the first investigation 93 miners were examined clinically and only those in whom signs of arthritis existed were submitted to X-ray of wrist and elbow. In 50 of these workers there were no symptoms. Among the remainder there were vasomotor symptoms in 32 chiefly of tingling and paraesthesia (25). Trophic changes existed in 4. Symptoms referable to the joints occurred in 31 miners but these were due to simple arthralgia in 21 of the men and definite arthritic changes were found in only 10 men—5 in the elbow, 4 in the wrist and 1 case of Kienböck's disease.

In the second investigation systematic X-ray examinations of wrist and elbow were carried out on 157 miners. The findings, which are set out in a table and discussed, were that definite arthritic changes were present in the elbow in 11, and in the wrist in 15 instances.

In the conclusion the opinion based on the findings of these 2 investigations is that although it is clear that there is a relation between the work with pneumatic tools and the articular lesions, nevertheless the resulting disability is by no means severe.

M. E. Delafield

SIMON, J. Verbreitung und Bekämpfung der Fussmykosen unter besonderer Berücksichtigung der Verhältnisse im Steinkohlenbergbau. [Distribution and Control of Foot Mycoses with special reference to Bituminous Coal-Mine Conditions] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete*. Berlin. 1960, May, v. 6, No. 5, 272-81, 5 figs. [44 refs.]

The author examined 1,625 mine workers at Zwickau, Germany for [unspecified] interdigital foot mycoses. In a 4 months' treatment, including spraying of patients'

feet and socks and of wash-, shower-, and cloak-rooms with the new antimycotic Brocona from VEB Chemische Werke, Radebeul, the incidence decreased from 61.23 to 24.06%. Of initially positive cases 77% were improved, 19.5 unchanged, and 3.5 deteriorated. It is maintained

that mass infection in large works can be rapidly controlled only by a combination of therapeutic and prophylactic methods, and the importance of the patients' co-operation and of the improvement of bathing and washing equipment is emphasized. *G. C. Ainsworth*

OCCUPATIONAL DISEASES

CARTWRIGHT, J. & SKIDMORE, J. W. **The Size Distribution of Coal and Rock Dusts in the Electron and Optical Microscope Ranges.** *Ann. Occup. Hyg.* London, 1961, Jan., v. 3, No. 1, 33-57, 13 figs. (2 on 2 pls.) [32 refs.]

In order to study the sizes of particles without the complication of atmospheric pollution, clouds of airborne dust were produced in the laboratory by abrading specimens of coal and rock in imitation of the rubbing, scraping, cutting and cleaving processes of mining. These were sampled by thermal precipitator and size distributions were constructed by using electron microscopy for particles below 2 microns and visual microscopy above 1 micron. Abrasion on dry and wet surfaces was studied.

The results are exhibited on log-log plots of the frequency, dN/dD , against diameter, D , since this often gives nearly straight lines over considerable ranges of D which were represented by the equation

$$dN/dD = KD^{-\gamma}$$

The value of K in this expression is arbitrary since it is determined merely by the total number of particles counted. γ , however, expresses the slope of the lines on the log-log plot and characterizes the size distribution. The larger the value of γ the greater is the relative preponderance of fine particles within the size range concerned.

Over a size range from 1 to 10 microns the value of γ was nearly constant for a given dust and varied according to the nature of the material and the method of dispersal. The same dusts gave lower values of γ over the size range 0.1-1 micron. The value of γ was not changed, in the case of a sandstone dust, by counting the individual particles in aggregates instead of taking them as units in the normal way. The effect of wetting a coal surface was to reduce to one-third of the dry value the particle frequency at 1 micron but little effect was produced at 0.2 micron.

Further experiments were undertaken with redispersed dust from the Soxhlet thimbles of Hexhlet dust sampling apparatus which had been run in two collieries. This dust had size distributions resembling the laboratory clouds of coal dust.

These experiments indicate a genuine reduction in the number of fine coal and rock dust particles below 0.1 micron.

Atmospheric pollution contains very few particles around 1 micron but a large number between 0.08 and 0.11 micron. It is thus confirmed that the rise in the number of fine particles in the ventilating air of coal mines is due to atmospheric pollution and not to the presence of fine dust from mining operations.

Samples of dust from dry percussion drilling in a quarry heading, under conditions such that atmospheric pollution did not obtrude, again showed a reduction in frequency of fine particles below 0.1 micron.

Dust produced by shotfiring in coal and rock, sampled from concentrations high compared with atmospheric pollution, indicated a decreasing proportion of fine particles with increasing airborne concentration. At low mass concentration a linear log-log plot extended to dust as fine as 0.06 micron whereas a deviation to lower frequencies occurred below 0.5 micron when the concentration was high. The mass proportion of ultra-fine particles was higher with coal than with rock. It is possible that the fine particles in the clouds produced by shotfiring were droplets of explosive fumes and, in the case of coal, droplets of volatile substances in coal which had been evaporated by the explosion and recondensed. Their appearance favoured this hypothesis and the smaller numbers seen at high concentrations could have been due to aerosol coagulation. *C. N. Davies*

ZURLO, N. **Counting of Atmospheric Dusts using Millipore Filters.** *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 660-71, 4 figs.

Difficulties in dust measurement with millipore filters include the poor visibility of small particles which is due to the refractive index of the liquid used to render the filter transparent being near to that of the dust, the gradual relapsing of the filter to opacity and the penetration of particles deeply into the filter if too much suction is employed.

A procedure is described which avoids errors due to such causes and gives results agreeing with those given by the thermal precipitator. The membranes were steeped in a mixture of methyl cellosolve and butyl alcohol for microscope counting which enabled particles of transparent minerals as small as 0.5 micron to be dealt with; transparency was retained for over 50 hours.

A special reversible mercury-displacement aspirator is described for use with the filters which sucks 100 cc. of air in a minute or two, depending on the grade of millipore, at a nearly constant flow rate. After the mercury has run from the upper into the lower reservoir, the apparatus is inverted and is ready for use again. Rubber diaphragm valves automatically apply suction and release air displaced from the lower reservoir.

(See *A reversible aspirator for the thermal precipitator*, WRIGHT, *J. Sci. Instr.*, 1954, v. 31, 263.)

C. N. Davies

HOCU-U. TIEFBAU. Zurich. 1960, Nos. 50/51, 10 pp., 6 figs. [Reprinted from.] Untersuchungen über die Ventilation von Stollen. I. Aufgabe und Ergebnis der Untersuchungen [Experiments on the Ventilation of Tunnels] [GESSNER, H. & STAHEL, M.]. II. Zusammenfassender Bericht über die Untersuchungen [Summary of the Investigation] [BÜHLER, H., SCHÄRER, P. & RUTISHAUSER, F.]

The tendency towards freer use of blasting and the mechanical transportation of the rock brought down has resulted in a speed-up of the rate of working when tunnelling. More fume and dust are produced than formerly and the method and rate of working form a better criterion of the amount of ventilation required than the number of men engaged.

The experimental conclusions which are described relate to tunnels of 6–12 m.² cross section and should not be applied to larger ones. Most of the paper is devoted to explosive fumes which are characterized by the explosive charge density, or ratio of the weight of explosive to the cross section of the tunnel, and by the length of the initial fume cloud which is of the order of 70 m. The carbon monoxide content, which is an index of amounts of various other gases, was 0.1–0.35% by volume in such clouds and the fine dust content was 300–500 mgm./m.³.

In assessing the risk of dust exposure, criteria due to Gessner are quoted. With 40% quartz in the rock a fine dust content exceeding 20 mgm./m.³ would cause silicosis. Between 10 and 20 mgm./m.³ would be liable to cause silicosis after long periods, such as decades. Below 5 mgm./m.³ even long exposure is not dangerous.

4 types of ventilation of a blind heading are analysed.

Suction ventilation through a pipe extending to within 12 m. of the face clears rapidly the cloud which lies outside the termination of the pipe but leaves relatively undisturbed the cloud between the orifice and the face; these are called zones B and A respectively. Suction ventilation can only be used when at least one hour work pause is allowed after blasting.

Pressure ventilation rapidly blows clear the fumes in zone A but everything travels through zone B and may result in the dangerous exposure of men working in other parts of the tunnel. At 20 times dilution of the initial cloud a visual impression of fresh air is obtained but, in fact, appreciable CO and dust remain, although in quantities not dangerous for a brief exposure.

Reverse ventilation is the most satisfactory method, especially for short tunnels. Pressure flow is used at first and reversed to suction just before blasting. This proceeds for a time interval calculated to ensure both the clearance of the outer zone, B, and the removal of fume from the duct. The flow is then reversed again and pressure used to sweep out the small, concentrated volume of fume in zone A at the end of the heading.

Formulae for calculating the times are given as well as worked examples.

Another system is to use suction throughout with a small supplementary duct to clean zone A. This duct is pressure fed and need only be short but care must be taken to see that it is switched on only when zone B, from which it draws air, is fresh.

If ventilation is satisfactory for dealing with blasting

fumes there should be no trouble with drilling or with carting rubble. Dry drilling raises a lot of dust and is forbidden. It should not even be used for a few seconds at the start of a hole.

C. N. Davies

RUTTNER, J. R. [M.D.] [Edited.] *Silicosis in Switzerland, 1945–1960*. [In German and English.] *Pathologia et Microbiologia*. 1960, v. 23, Suppl., pp. ix + 150. New York. Basle: S. Karger, Arnold-Böcklinstr. 23–25, Switzerland. [Sw.fr. 15.-]

In 1944 the Zurich Research Group for the investigation and prevention of silicosis in Switzerland was established. The Group is divided into an "inorganic" and a medical section with divisions concerned respectively with minerology, pathological anatomy, clinical studies, radiology and the work of the Swiss National Accident Insurance Fund. It is not, however, a centralized institute for silicosis research and each member of the Group—usually a director of a clinic or institute—carries out his own investigations. In the present volume 107 Scientific Studies undertaken during the years 1945–60 are abstracted in German and in English and the book has 5 sections each representing the work of a division of a Group. Although 58 individual authors are listed, the investigations have clearly in general been carried out under the direction of the chief of the particular institute in which the work has been done. Thus in the section of pathology there are 39 abstracts and Professor Rüttner is himself author, or part author, of 32.

Since medical studies on silicosis rarely furnish exact data on the dust conditions of the environment, the 11 papers abstracted in the mineralogical section are chiefly directed towards the technical aspects and furnish the foundation for preventive measures in dust control. Under the heading of pathology most of the abstracts are concerned with the investigation of basic factors in silicosis and animal experiments proved to be of great value. Intraperitoneal tests in fact were first developed in Professor Rüttner's institute where these studies were carried out. The field covered is wide and includes investigations into the effects of the inhalation of graphite and grain dust. Experimental work is presented indicating the validity of the assumption that dust containing no quartz can cause pneumoconiosis. Other studies assess critically the solubility and the immunological theories of silicosis. There are also abstracts on work dealing with the aetiology of cor pulmonale and bronchitis and pulmonary emphysema in relation to pneumoconiosis.

The clinical section contains the abstracts of 15 papers and in addition there is a synopsis of a monograph of 395 pages entitled *Physiologie und Pathophysiologie der Atmung (Physiology and Pathophysiology of Respiration)* by P. H. ROSSIER, A. BÜHLMANN and K. WIESINGER. Professor Rossier is the senior author of this work and is also responsible in part or in whole for 11 of the 15 abstracts which are mainly devoted to tests of lung function. 10 abstracts are included under the roentgenological section: as well as general studies on the X-ray appearances in silicosis, investigations of a more specialized kind have also been undertaken, for example

on the experience gained from bronchography in silicosis, and there is a report of experimental work on the effect of quartz and glass dusts in the anterior chamber of the rabbit's eye.

In the section dealing with papers concerning the Swiss National Accident Insurance Fund, there are 33 abstracts comprising a certain number of administrative problems but mainly dealing with general considerations, prevention and the incidence of silicosis in various industries and in different parts of Switzerland.

The work abstracted in this volume is most comprehensive and includes much fundamental research; however, since it is basically a collection of abstracts of papers by many authors from various centres, it is not surprising that conflicting statements sometimes appear. Thus in the introduction to the clinical section the association of tuberculosis with silicosis is said to be a rarity while in a study abstracted in the final section the author claims that silico-tuberculosis is found in no less than 23% of the lungs of foundrymen, which he compares favourably with the 60% of silico-tuberculosis found "in other species of silicosis".

Only a few of these papers have previously been abstracted in this *Bulletin* and this book therefore will be of much value to workers engaged in the study of silicosis who may not previously have had ready access to the work of the Zurich Group. It may be added that the abstracts have been rendered in excellent English.

G. F. Keatinge

PIAZZA, G. & PICOTTI, G. Esame radiologico di mille casi di silicosi. Considerazioni sulla classificazione (secondo la convenzione internazionale di Ginevra), sulle compromissioni ilari e sulle atelettasie. [Radiological Examination of 1,000 Cases of Silicosis. Remarks on Classification (according to the Geneva International Convention), Hilar Involvement and Atelectasis] *Med. d. Lavoro*. 1960, Dec., v. 51, No. 12, 804-25, 11 figs. [Numerous refs.] English summary.

This article opens with a critical review of the pathological anatomy in silicosis and the authors find the immunological explanation proposed by VIGLIANI and his co-workers to be the most satisfying theory of its cause. Although morbid anatomy and the radiological appearances cannot with certainty be correlated with each other, nevertheless the need for a standard classification is emphasized since only by this means can the findings of one worker in this field be compared with those of another. The Geneva classification proposed by ILO in 1958 has been adopted in this survey.

1,089 cases of silicosis were investigated and the distribution data were L=9.27%, p=32.60%, m=25.90%, n=7.53%, conglomerate=24.7%. An "n" background was commonest in the conglomerate forms. Positive sputum was present in 4.32% of cases. Hilar involvement was found in 40.31% of cases. 3 criteria were used, namely, simple enlargement of the hilar shadow, enlargement of lymph nodes, and enlargement of lymph nodes with calcification. Hilar enlargement was most frequently seen with type n opacities: the more uniformly dense type of lesion was associated often with

conglomerate and n opacities than with others. In silico-tuberculosis hilar enlargement was met with in 36.36% of cases. Obstruction to the airways was noted in 15.34% of cases and was more frequent in patients with hilar involvement (27.33%) than in others (7.23%). Middle lobe atelectasis was present in 30 cases (2.76%). The total duration of exposure did not seem to influence significantly the distribution of radiological pictures nor did there seem to be any relation between duration of exposure and degree of atelectasis or hilar involvement. No significant difference was found between men who had worked only in rock and those whose exposure had been of mixed type. Cases from the iron and steel industry presented almost entirely with types p and m and hilar calcification was less frequent.

The importance of individual susceptibility and of superimposed infection is stressed.

The rare occurrence of hilar calcifications in silico-tuberculosis (1.51%) as compared with the frequency in the whole survey (6.43%) suggests that hilar calcifications may be characteristic of silicosis, independent of the presence or absence of any specific association. As regards the pathogenesis of atelectasis, in addition to bronchial occlusion from pressure due to enlarged lymph nodes other possible factors are discussed. It is suggested that the symbol At (relative to atelectasis) be adopted as one of the additional symbols of the classification. The importance of specialized radiological methods (e.g., tomography, bronchography) is stressed, with particular reference to adenopathies and atelectasis.

G. F. Keatinge

BELLINI, F. & GHISLANDI, E. Calcificazioni "a guscio d'uovo" a sede extrailare in silico-tubercolotico. [Extra-Hilar Eggshell Calcification in a Case of Silico-Tuberculosis] *Med. d. Lavoro*. 1960, Oct., v. 51, No. 10, 600-606, 5 figs. [19 refs.] English summary (6 lines).

After having met with a case of silico-tuberculosis in which there was eggshell calcification of many lymph nodes in the lungs, in the intercostal spaces, and in the anterior and posterior mediastinum, the authors studied the X-rays of 1,905 silicotic subjects who had been admitted to the Clinica del Lavoro in Milan during the period 1945-60. Eggshell calcification was seen in 90 films (88 men and 2 women) which is equivalent to an incidence of 4.7%. In 83 cases the condition was present on both sides: in 5 only on the left and in 2 only on the right. Eggshell calcification was restricted to the hilar and parahilar regions in all 90 cases which accords with the findings of previous authors save for RIEMER (*Amer. J. Roentgenol.*, 1945, v. 53, 439) and JACOBS *et al.* (*Radiology*, 1956, v. 67, 527), who reported eggshell calcification in the peri-aortic glands.

In a review of earlier literature the incidence of eggshell calcification is quoted as ranging from 35% in a series of 114 silicotic subjects [GRAYSON and BLUMENFELD, 1949, *Radiology*, v. 53, 216] to 0.2% in 4,000 examinations by FOUBERT *et al.* [this *Bulletin*, 1952, v. 27, 941]. However, the present survey resulted in a percentage not greatly different from the 3% recorded by ZANETTI in an earlier survey made in the Clinica del

Lavoro, Milan, in 1946 (*Med. d. Lavoro*, 1946, v. 37, 131). This is the only investigation in which a sufficiently large number of subjects has been studied.

Although widespread and obvious parenchymatous calcification has been noted in various chest conditions by other authors, it has only been seen when the lung itself has been involved, whereas in the case now described calcification was strictly localized to the glands themselves and their immediate neighbourhood.

G. F. Keatinge

LAVENNE, F. & PATIGNY, J. Valeur comparée de la radiographie et de la radiophotographie pour le diagnostic de la pneumoconiose des houilleurs. Étude expérimentale. [*An Experimental Study of Comparative Value of Full-size and Miniature Radiographs in the Diagnosis of Coalworkers' Pneumoconiosis*] *Rev. Inst. Hyg. des Mines*. Hasselt. 1960, v. 15, No. 4, 115-34. [40 refs.]

[The identification of minimal radiographic changes is an important item in the diagnosis of early pneumoconiosis. Since the original study by FLETCHER and OLDHAM in 1949 (this *Bulletin*, 1949, v. 24, 971) many investigations have confirmed that there can be considerable intra- and inter-observer error in the interpretation of the same radiographs at intervals of time by observers, individually and collectively.

In Great Britain it is generally accepted that for the early diagnosis of pneumoconiosis miniature films (photo-fluorographs) are inadequate. By contrast in some countries on the continent of Europe miniature films are used particularly for periodical examination of workmen in dusty occupations. It is argued that when viewed by experts these films are adequate and have the merit that they are considerably cheaper than full-size film. These matters were deliberated (*ibid.*, 1960, v. 35, 21) by the experts who devised the current International Classification of Radiographs of the Pneumoconioses at Geneva in 1958. Indeed, they recommended that comparative tests should be made with large and small films (*loc. cit.*)]

The purpose of this Belgian study was to compare the value of miniature films with full-size films in the diagnosis of simple pneumoconiosis in coalworkers, particularly at the level of category 1.

16 physicians with specialist experience of pneumoconiosis among coalworkers were asked to classify, on 2 occasions at an interval of 2 weeks, the radiographs of 50 coalworkers. Films were made of each subject on 3 sizes of film, 35 cm. × 35 cm. (full-size) and 10 cm. × 12 cm. and 7 cm. × 7 cm. The large films were read without reference to standard films.

The results are presented in the now familiar box matrix tables in general use for studies involving intra- and inter-observer error. It was found that small films are significantly less reliable for accurate diagnosis than large films. There is, however, little to choose between 10 cm. × 12 cm. and 7 cm. × 7 cm. Whatever size of film used, high-grade technique is of primary importance. The cause of *observers' dispersion* [reviewer's italics], it is submitted, may be due to physiological and psychological factors which merit experimental study.

[The authors, as quoted, refer to "observer dispersion". The original term was "error" but recently there has been a tendency to criticize this as implying a mistake. Apparently for this reason there has recently been a change of nomenclature to "observer difference", "variation" and "deviation". Etymologically, "error" is appropriate, *errare* meaning to wander or stray.]

A. Meiklejohn

NAGER, F., ZENGER, F. & RÜTTNER, J. R. Bronchitis, Bronchiolitis und Silikose. [*Bronchitis, Bronchiolitis and Silicosis*] *Schweiz. med. Woch.* 1960, Nov. 26, v. 90, No. 48, 1357-64, 1 fig. [66 refs.]

The various views on the relationship between bronchitis and silicosis are discussed in the first part of this paper under the headings of statistical investigation, investigation by bronchoscopy, experimental research and pathological investigation. The authors' contribution falls into the last category. They investigated histologically 100 lungs from 36 subjects with classical silicosis, 17 from subjects exposed to mixed dust and 47 from subjects with silicotuberculosis. These were compared with 30 lungs of patients dying of primarily non-pulmonary conditions, where the patients had been bed-fast with stasis of the lungs. 20 lungs from subjects with bronchitis and emphysema were also used as controls.

The result of the investigation was that there was considerable inflammatory change in the bronchi and bronchioles in all stages of silicosis. These changes were not found or were not so definite in the controls. In the bronchi of the silicotic lungs there was a lymphoplasmacellular infiltration, there were signs of hypersecretion, atrophy of the elastic tissue and later of the muscular tissue, sometimes bronchostenosis and bronchiectasis. The cilia were intact. In the bronchioles, the conditions were more marked. The silicotuberculosis cases showed the same changes in areas away from tuberculous foci. The changes were found in all stages. The bronchiolitis and bronchiectasis were essentially dependent on dust. They were analogous with the bronchiolitis deformans of the later stages and might be termed bronchiolitis deformans pneumoconiotica. With increasing severity of the silicosis the bronchial and bronchiolar changes were more definite. The fact that many severe cases of silicosis present no clinical evidence of bronchitis is to be explained by the fact that the bronchitis is "hidden" by the silicotic masses.

The conclusion is that in the early stages along with the bronchitic syndrome acting as a protective mechanism during the exposure, there is true bronchitis and bronchiolitis. While in the large bronchi the defensive mechanism predominates, in the small bronchi and in the bronchioles there is a true inflammation outlasting the dust exposure. The retention of dust in the bronchiolar wall leads to bronchiolitis. This favours the retention of dust, bacteria, etc., as well as secretion, cell debris, pus, etc. This retention limits dust elimination and, so long as exposure lasts, favours the progress of silicosis. It also increases the probability of infection, even after the cessation of exposure. The results also

indicate that younger silicotic subjects tend to have bronchitis more severely than older patients. The presence of bronchitis in silicosis should not be considered merely as senile bronchitis. *Charles L. Sutherland*

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **Tuberculosilicosis: a Study of its Synergistic Mechanisms.** *J. Occup. Med.* Chicago. 1960, Dec., v. 2, No. 12, 571–5, 13 figs.

The mechanism of the combined action of tubercle bacilli and silica in the production of tuberculosilicosis—or more generally complicated pneumoconiosis—is not yet understood. Until now KETTLE’s hypothesis (*Brit. J. Exper. Path.*, 1924, v. 5, 158) that the silica retained in the lungs provided a favourable medium for the implantation and growth of tubercle bacilli has predominated. The recent hypothesis of VIGLIANI and PERNIS [this *Bulletin*, 1961, v. 36, 1] postulating an immunological basis for the pathogenesis of silicosis has excited re-examination of the problem of tuberculosilicosis.

At the Mellon Institute, Pittsburgh, Pa., Gross *et al.* have carried out a programme of laboratory investigations including experimental tuberculo-pneumoconiosis [this *Bulletin*, 1959, v. 34, 781] and the pulmonary response to tuberculin [*ibid.*, 1961, v. 36, 294]. The present report is the latest in the series.

Guineapigs were rendered tuberculin positive with a subcutaneous injection of a strain of tubercle bacilli, which was only weakly pathogenic for this animal. After demonstration of a positive tuberculin reaction some of the animals were given one or more intratracheal injections of quartz, with or without tuberculin, and tuberculin alone. The scheme is summarized in the following table:

Experimental Set-Up of Intratracheally Injected Tuberculin-Positive Guinea-pigs

Group	No. of Single or guinea-multiple pigs dosage		Total Dosage (mgm.)	
			Quartz	Tuberculin
Tuberculin with quartz dust	30	S	50	0.01
Tuberculin with quartz dust	30	M	150	0.03
Tuberculin alone	15	S	—	0.01
Tuberculin alone	15	M	—	0.03
Quartz dust alone	15	S	50	—
Quartz dust alone	15	M	150	—

Several animals died of pneumonia; the remainder were killed at intervals up to 13 months. The aim was to study the progress of tissue changes in the lungs. These histological changes observed in the separate groups are described and illustrated by photomicrographs.

The authors submit that “the modification of experimental silicosis by an immune reaction, as exemplified by the pulmonary tuberculin reaction, supports the hypothesis that the development of tuberculosilicosis is dependent upon a reciprocal stimulation of tissue responses caused respectively by silica dust, on the one

hand, and by sensitivity to the tubercle bacillus and its products on the other, as postulated by Vigliani and PERNIS”. *A. Meiklejohn*

MOSINGER, M., FIORENTINI, H., GRAS, A., GARČIN, C., EL FEKI, M. & CARTOUZOU, G. La silicose expérimentale du chien. [Studies of Experimental Silicosis in Dogs] *Arch. Malad. Professionnelles*. Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 5–39, 51 figs. [11 refs.]

Experimental studies of silicosis in the laboratory have largely been carried out in small animals such as rats, guineapigs, hamsters, and mice. While for certain observations, pathological and epidemiological, these animals have advantages, their size considerably restricts the range of investigations. Mosinger and his colleagues decided to use dogs for their experiments. Under intravenous anaesthesia, suspensions of powdered quartz (size under 3 microns) in isotonic serum were injected into the lungs or selected lobes of these through a bronchoscope. 34 dogs [breeds not indicated] were given single or multiple doses at intervals. The survivors were observed over periods from 9 to 32 months. The investigations comprised clinical, radiological (including tomography and bronchography), metabolic, biochemical, morbid anatomical and surgical excision. The results are described very fully under these headings and illustrated by photographs of specimens and photomicrographs.

It emerges that the features of the disease in the dog approximate closely to those observed in man. The onset of emphysema, it is remarked, is precocious. The authors submit that their findings prove that silicosis affects not merely the lungs and hilum glands but also other organs, and that the accompanying biochemical changes signify systemic changes. Finally the merits of the dog for experimental work in pneumoconiosis are emphasized. *A. Meiklejohn*

HARLEY, J. D. & MARGOLIS, J. **Haemolytic Activity of Colloidal Silica.** [Correspondence.] *Nature*. 1961, Mar. 25, v. 189, 1010–11, 2 figs. [11 refs.]

Colloidal silica of particle size 30 $m\mu$ in a concentration of 1 $\mu\text{gm./ml.}$ lysed 50% of a 2% suspension of washed erythrocytes. The surface area of the erythrocytes was more than 150 times as great as that of the silica in these conditions. Silicic acid or silica preparations in the range 3.5–7 $m\mu$ agglutinated erythrocytes with a prozone effect but cells treated with particles of 3 $m\mu$, or smaller, were not susceptible to agglutination or haemolysis by larger particles and exhibited a number of other interesting properties. Tentative suggestions are made as to the mode of action of silica on the surface of erythrocytes. *J. Marks*

BARGHINI, G. L'abbattimento delle polveri prodotte durante la lavorazione della pietra per la produzione della dolomite sinterizzata in polvere e durante la macinazione della pietra. [Control of Dust Produced during the Sintering of Dolomite and in Grinding Operations] *Riv. Italiana d'Igiene*. 1960, Sept.-Oct., v. 20, Nos. 9/10, 380-94, 8 figs. English Summary.

In the course of the sintering of dolomite dense concentrations of dust which polluted the atmosphere in the neighbourhood of the works at Torano in Carrara were controlled by the provision of expansion chambers fitted to the top of the furnace chimney. The dust created on removal of the sintered material from the furnace is drawn off through a cyclone and collected in a closed chamber.

The crushing, grinding and grading are also accompanied by much dust formation and for the larger particles exhaust ventilation and a cyclone suffice. To eliminate the smaller particles under 15μ in size a system has been devised for bubbling the dust through water which allows the solid material to sink to the bottom of the apparatus, which is cleaned out from time to time.

Crushing and grinding of dolomite and marble into powder is also a dusty operation and in it the larger particles are suppressed by means of a special exhaust system and cyclone. The apparatus is known as a micro-cyclone and makes use of combined centrifugal force and of the resistance to the particles which takes place when they come into contact with the walls of the ducting.

Transport of material from the meshes to the grinding machine creates dust and in order to control it a closed system of oscillating cylindrical metal tubes is used to convey the product from one machine to the other. The operations from this point until final bagging, are completely enclosed.

[Constructional details are lacking so that it is only possible to form a general impression of the methods described.]

G. F. Keatinge

JACOB, G. & BOHLIG, H. Das Verhalten des Bronchialbaumes bei der Asbestlungenfibrose. [The Changes in the Bronchial Tree in Asbestosis] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 247-57, 7 figs. [Numerous refs.]

This bronchographic study of various stages of asbestosis has been facilitated by the use of a new contrast medium—propylidone. In asbestosis with thickening of the pleura the small bronchi towards the base are bunched together with their ends turned back. This was described by JACOB (*Bronchographische Befunde bei der Asbestlungenfibrose*, Verh. Ber. 41, Tagg der Dtsch. Röntgenenges., 1960, Freudenstadt) as the "broom phenomenon" and is associated with displacement of the basal segments of the lung. This is not pathognomonic for asbestosis since it occurs in other conditions causing pleural thickening. In all cases the conditions grouped under the term "bronchitis deformans" are to be found. The distension of the bronchi expected from the character of the disease is evident but bronchiectasis is not so

striking as in silicosis even in advanced asbestosis and it is cylindrical in type. In contrast to silicosis, there is no stenosis of the large bronchi.

The reabsorption of the contrast medium is delayed in 25% of the cases, a sign of interference with the pulmonary circulation. In pneumoconiosis the connective tissue masses tend to contract and to scar and this leads to distortion of the bronchial tree. This distortion gives rise to a characteristic sign, the bunching of the segments of the bronchi supplying the fibrotic part of the lung; while the branches of the bronchi of the less fibrotic parts are spread apart in compensation. In asbestosis as a rule the lower and middle lobes, and in the left lung the lingula, are affected, and in silicosis the upper lobe. In these lobes the bronchi are bunched while in the other lobes they are spread out.

In asbestosis the normal appearance of the bronchus next to the hilus can be seen but this is not so in silicosis where there is increase of the lung roots and obliteration of the lymph apparatus. The swelling of the roots may be so massive that many authors believe that silicotic patients with carcinoma of the lung have a greater expectation of life because of the closure of the way for metastasis [SMITH, this *Bulletin*, 1960, v. 35, 855]. This very questionable assurance is not granted to the asbestosis patient.

Charles L. Sutherland

CLARK, S. G. & HOLT, P. F. Studies on the Chemical Properties of Chrysotile in relation to Asbestosis. *Ann. Occup. Hyg.* London. 1961, Jan., v. 3, No. 1, 22-29, 2 figs. [10 refs.]

There are 2 rival hypotheses, mechanical and chemical, of the pathogenesis of asbestosis. According to the chemical hypothesis the fibrosis of the lungs is due to the action of silicic acid derived from the decomposition of asbestos in the lungs. This report describes studies made at the University of Reading, England. The experiments were made *in vitro* and the aim was to discover the rate of dissolution of South African chrysotile asbestos at temperatures between 25° and 90°C . in neutral, acid and alkaline media. The media used were respectively water, 0.1N hydrochloric acid and 0.1N sodium hydroxide. The analyses of the extracts at various intervals of time are tabulated.

It was observed that the dissolution resulted in the removal of magnesium [the empirical formula of chrysotile is $\text{Mg}_3\text{Si}_2\text{O}_5(\text{OH})_4$] and "the release of minute, two-dimensional 'flakes' of the silica lattice". From this it is deduced that a reaction similar to that normally evoked by fine silica particles would follow.

Dissolution, it was observed, occurred more readily with alternating acid and alkaline conditions than under the influence of acid or alkali alone. Such an alteration of acid and alkaline states occurs in inflammatory diseases including pneumonia and bronchitis. The authors conclude that if the breakdown of chrysotile follows the same course *in vivo* as it does *in vitro*, a pneumoconiosis having a general resemblance to silicosis would be expected.

[With reference to this conclusion it can be asserted with almost absolute assurance that, viewed from the

clinical, radiographic, morbid anatomical and pathological aspects of the disease in men and women, there is practically no similarity between silicosis and asbestosis.]

A. Meiklejohn

SANO, H. [Studies on the Asbestosis Body] *J. Sci. of Labour*. Tokyo. 1961, Jan., v. 37, No. 1, 16-28, 5 figs. [23 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"A clinical and experimental study was made on the asbestosis body, and the following results were obtained.

"1) Asbestosis body was found in 40.1% of 147 sputum specimens taken from employees in an asbestos factory. It was found in higher rate in accordance with the development of roentgenographic appearance and the prolongation of employment. The rate of detection was higher in cases with advanced inflammation of bronchi and was increased by frequent examinations.

"2) The bodies seemed to be classified into the following 5 types in their shapes and process of the formation: club or rod shape (type A); dumb-bell shape (type B); a segment form (type C); beads or necklace like form (type D); and more complicated form due to the process of its destruction (type E).

"3) The bodies were destroyed by addition of concentrated sulfuric acid or hydrochloric acid, but no remarkable changes were caused by heating (180°C for half an hour) or addition of concentrated alkaline or proteolytic enzymes.

"4) The production of the asbestosis body in the peritoneal cavity and the subcutaneous tissue of guinea pigs was unsuccessful, but the production of typical beads like shaped bodies were noted in the pleural cavity 10 weeks after inoculation of asbestos fibres.

"5) The asbestosis bodies were found in the lungs of animals which were treated with antiformalin for 48 hours or more, and the shortest time required for their formation was 4 weeks in guinea pigs and 7 weeks in rats after the inhalation of asbestos fibres. The follow-up observation on the process of formation of asbestosis bodies in animal experiments approved the assumption on the development of asbestosis bodies induced by the observation of asbestosis bodies in the sputum specimens of asbestos workers."

ROBERTSON, A. J. & WHITAKER, P. H. **Radiological Changes in Pneumoconiosis due to Tin Oxide.** *J. Facul. Radiologists*. 1955, Apr., v. 6, No. 4, 224-33, 17 figs.

The authors (who wrote from Liverpool) examined radiologically 215 employees from a tin-smelting works, finding, in 121, abnormalities which ranged from faint early mottling to gross dense nodulation. There were also linear opacities, presumably due to dust deposits in sub-pleural lymphatics. The opacities were always discrete, and there was no coalescence.

The raw ore is cassiterite, mainly tin oxide, which

comes in bags which are emptied by hand, and in the men who do this work the lung changes are particularly marked, varying with length of exposure. Men working in the calcining shed are not much affected, but those in the smelting furnace house are more so, and those in the refinery furnace work, where much dust is raked off, are extensively affected. The two important factors are quantity of dust and length of exposure.

Clinically the condition is benign, and all the men were well, without complications. Tin does not seem to be locally reactive in the lung, and its high atomic weight renders it very radio-opaque, so that inhalation of small quantities of respirable size may result in radio-opacity which should enable a diagnosis to be made early; there may be less dust in the lungs than in those of a young coal-miner, but the extreme density of tin gives a typical X-ray picture long before the relatively non-opaque coaldust.

There are 17 reproductions of X-ray films of the lungs. [See DÉROBERT *et al.*, below.]

Charles Wilcocks

DÉROBERT, L., HADENGUE, A., LE BRETON, R., ABRIC, J., GIROULLE, H. & FÈVRE, J. C. **Pneumoconioses à l'étain. [Pneumoconiosis due to Tin]** *Arch. Malad. Professionnelles*. Paris. 1960, Dec., v. 21, No. 12, 713-18, 2 figs. [10 refs.]

On resuming work after an acute respiratory illness a workman was submitted to radiographic examination of the chest. The X-ray revealed a generalized miliary nodulation of the lungs. This finding appeared anomalous as a variety of tests proved that the workman was in excellent health. On enquiry it was discovered that for the previous 11 years he had been employed at a small factory in the production of tin oxide. The atmospheric conditions were described as very dusty and on occasion he had suffered slight shortness of breath on exertion. Arrangements were made for the X-ray examination of his 5 workmates and this revealed 3 similar cases of micronodulation of the lungs. 3 former employees were traced but only 1 was alive and his lungs showed the same X-ray changes. The authors then made a study of the literature on the effects of the inhalation of tin dust. They also carried out an experimental study by "dusting" guineapigs. As a result of all the investigations it was concluded that the inhalation of tin results in a benign pneumoconiosis, characterized radiographically by dense micronodulation of the lungs but causing no impairment of pulmonary capacity. Two other features are mentioned: a greyish metallic tinge of the sputum and bradycardia.

[Commenting on the 121 cases detected in a survey at Liverpool in 1955 by ROBERTSON and WHITAKER [see above] the present authors state that in their opinion the overwhelming majority of those cases were true silicosis, or more precisely silico-stannosis. It is important that readers should understand that this opinion is erroneous, as will appear by reference to the chapter on *Pneumoconiosis due to Tin Oxide* by A. J. ROBERTSON in *A Symposium on Industrial Pulmonary Diseases*, this *Bulletin*, 1960, v. 35, 1172.]

A. Meiklejohn

PLAMONDON, S. R., EL-DAKHAKHNY, A. A., ABDEL SALAM, M. S. & VALIC, F. **Dust Exposures and their Control in Iron Mines of Aswan.** *J. Egyptian Pub. Health Ass.* 1960, v. 35, Nos. 4/5, 155-64.

A description is given of dust conditions in the mining and crushing of iron ore at Aswan. About 490 workers are employed in mining which is by open cast methods, and 40 to 50 on each of 3 shifts at the crushing plant 25 km. distant. The free silica content of the dust in the mining area was 37% and at the crushing plant 26% ascertained chemically; by petrography the results were lower. Dust concentrations were almost unbelievably high: 80% of all samples taken gave results higher than 20 million particles per cubic foot [m.p.p.c.f.] (the MAC for dust containing between 5 and 50% free silica), and, at the crushing plant, 83% of all samples were higher than 50 m.p.p.c.f. Some median concentrations expressed in m.p.p.c.f. were 3,015 during unloading down wind, 2,061 in the crusher feeding tunnel, 331 at car loading, and 154 at crushing and grading. In the crusher feeding tunnel the minimum count recorded was 695 m.p.p.c.f., nearly 35 times the MAC, and the maximum was 8,064 m.p.p.c.f. Only particles less than $5\ \mu$ were counted. Of these, 60% in the mining area and 88% at the crushing plant were less than $1\ \mu$.

No clinical or X-ray examinations of workers are reported and there is no reference to cases of pneumoconiosis, but the pressing need for dust suppression is realized and methods of achieving this are discussed. The major difficulty at the mines is the complete lack of water in the vicinity. At the crushing plant water is available and by its use, together with enclosure and local exhaust ventilation at dusty points, and vacuum cleaning, considerable reduction in dust concentrations should be achieved.

A. T. Doig

MEIKLEJOHN, A. **Visit to Crushing Plant at Aswan, 21-24 March, 1960. Commentary.** *J. Egyptian Pub. Health Ass.* 1960, v. 35, Nos. 4/5, 165-8.

The author comments on a visit he paid to the crushing plant described in the foregoing abstract. The fine red haematite dust was inescapable, soon covering clothing and staining nasal passages, mouth and throat. Plant buildings, houses and roadways were thickly covered, and a cloud of dust was blown far and wide from a huge tip. The risk to health from pneumoconiosis was obvious and there was evidence that several workmen were already affected after 2 years' employment.

New crushing plants will be required to meet the demand for steel, and although engineering control of the dust does not seem to be possible at this plant, it must continue to operate. It is therefore essential that the experience gained must be applied to ensure that new plants are designed, constructed and maintained to eliminate the dust hazard.

So far as the present plant is concerned, medical supervision will have to be the main measure in safeguarding health. This can only be palliative, and leading to suspension of those affected at the earliest stage. To this end a full-time works medical officer was recently

appointed. The author advocates the development of present medical arrangements and the maintenance of a research project to provide basic medical and engineering knowledge. To safeguard the health of the present workers, the method of short term employment seems inescapable; it is suggested that the aggregate period for employment in the dustiest situations such as the tunnel should not exceed 12 months.

A. T. Doig

FRIEDE, E. & RACHOW, D. O. **Symptomatic Pulmonary Disease in Arc Welders.** *Ann. Intern. Med.* 1961, Jan., v. 54, No. 1, 121-7, 3 figs.

The authors describe the case of a 40-year-old white male who had worked continuously as an arc welder from 1945 to 1956 and previously for short periods amounting to a few months while engaged in construction work on farms before the Second World War. When seen in hospital in 1956 he complained of having suffered from weakness and shortness of breath for 2 years and ankle swelling for 6 months. He was cyanotic and very dyspnoeic. In addition to abnormal signs in the heart and lungs, enlargement of the liver and oedema of the legs extending to the knees, there was severe polycythaemia. The haemoglobin value was 26.1 gm. per 100 cc., the red cell count 7.5 million per cmm., and the haemocrit reading 72%. The arterial oxygen saturation was 46%, the red cell mass being 441% of normal. Pulmonary function tests showed a vital capacity of 1.5 litres, this being 36% of the predicted normal, and the maximum breathing capacity 24% of normal. The ventilatory pattern suggested marked obstruction. X-ray examination of the chest showed diffuse pulmonary fibrosis with severe emphysema.

Histological examination of a biopsy specimen of lung tissue showed macrophages loaded with brown pigment in the alveoli and interstitial tissue, thickening of the septa and diffuse fibrosis. The Prussian blue test showed that the pigment was iron. Analyses of a welding rod, its coating, and of the fume generated during welding showed that silica was present.

The case is presented as one of pulmonary fibrosis and advanced emphysema, with secondary polycythaemia, pulmonary hypertension and right-sided heart failure, due to the inhalation of arc welding fumes containing a combination of iron and free silica. [It seems more probable to the reviewer that the severe polycythaemia is the primary condition in this case, the pulmonary features being secondary, but this possibility is not discussed by the authors.]

[See also this *Bulletin*, 1936, v. 11, 524; 1954, v. 29, 61; 1955, v. 30, 879; 1956, v. 31, 923.]

A. T. Doig

SALFELDER, K. **Über die Bagassestaublunge mit Bericht über einen Sektionsfall. [Bagassosis; with a Report of an Autopsy]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 233-46, 5 figs. [29 refs.]

In describing the process of extracting sugar from sugar cane the author draws attention to the conditions under which the by-product, bagasse, is stored. Bagasse

is often left in the open air exposed to the sun. It is initially moist and still contains a little sugar and so provides a good culture medium for moulds. In time it crumbles, and when it comes to be transported and used as fuel for firing boilers, or as manure on the land or for paper making, it readily gives off clouds of dust.

The literature only provides 4 cases of bagassosis where pathological studies were made and in only one were foreign bodies found in the lung tissue, and these were interpreted as derived from bagasse because of the history of exposure. The literature quoted includes SODEMAN and PULLEN [this *Bulletin*, 1944, v. 19, 773], HUNTER and PERRY [*ibid.*, 1946, v. 21, 747], CASTLEDEN and HAMILTON-PATERSON [*ibid.*, 1943, v. 18, 134], but it is stated that these contributions were not studied. In chronic lung disease such as farmer's lung and bagassosis, the offending material may disappear from the tissue.

The author's case was of a man aged 28 who died after 10 days of a respiratory illness which commenced with high fever and rigors. The industrial history is not clear but the man worked in a sugar factory. The pathological diagnosis was lobar pneumonia. The histology indicated a slight fibrotic reaction to a mixed dust but the alveoli of most of the lung were filled with exudate, leucocytes, erythrocytes and alveolar cells, and in some areas there were granulomata with epithelioid cells surrounding the exudate. With ordinary stains no bacteria or foreign bodies are found but with the Grocott-Gomory-methenamine silver stain (*Manual of Histology*, 1957, Washington D.C., Armed Forces Institute of Pathology), under the oil immersion lens structures of various forms and sizes were revealed, which must be interpreted as portions of mould; many types are found in the dust of bagassosis. In this case, a mixed dust inhalation had given rise to a chronic fibrosis, the granulomata and the bilateral acute pneumonia were caused by a mould.

Charles L. Sutherland

HESS, J. W. **Lead Encephalopathy simulating Subdural Hematoma in an Adult. Report of a Case.** *New England J. of Med.* 1961, Feb. 23, v. 264, No. 8, 382-4. [16 refs.]

Until carotid arteriograms 5 days after admission showed no abnormality, the course of headache, convulsions, coma and localizing neurological signs was attributed to a fall 2 days before: the patient, aged 40, was an alcoholic. After infusions containing vitamin B, he was able to mention work with lead, but convulsions then became more severe. Deviation of eyes and head to the left was followed by left-sided twitching, tonic-clonic movements of the left arm and spread to the right, with abnormalities of reflexes. The illness, treated by sedation and antibiotics for aspiration pneumonia, remained critical. Meanwhile investigations showed anemia, leucocytosis, 18 stippled cells per 1,000 red cells, and raised blood urea and cerebrospinal fluid protein, the fluid being under increased pressure. The encephalogram showed diffuse slow activity, with no localizing changes. Other examinations were within normal limits.

EDTA was given intravenously on the 6th day and there was only 1 further convulsion. After 3 gm. daily

for 3 days the urine contained 7.25 mgm. Pb, and 516 μ gm. coproporphyrin, per 24 hours. The patient became responsive, and was ambulatory a fortnight later with no peripheral neuropathy. Meantime the cerebrospinal pressure had become normal and later so did the protein and the blood urea. There were no symptoms on discharge 1 month after admission. The total dose of EDTA was 29 gm. in 2 courses of 1 week's duration. Symptoms had followed the time response reported in EDTA treatment of children with Pb encephalopathy [this *Bulletin*, 1957, v. 32, 548].

The patient had melted Pb, obtained by breaking open old batteries, into piggots for 6 months previously. He had had abdominal cramp, headache, dizziness and dyspepsia for 3 weeks before falling. There may have been more than a coincidental relation between alcoholism, minor head injury and the appearance of the lead encephalopathy which, though rare in adults, should be remembered in the diagnosis of cerebral disease, since it can be treated.

M. Patricia Fitzsimons

THOULD, A. K. (for ASHBY, M. G.) **Lead Encephalopathy.** *Proc. Roy. Soc. Med.* 1961, Mar., v. 54, No. 3, 228-9 (Clin. Sect. 2-3).

Report of a case.

ZIELHUIS, R. L. **Coproporphyrinuria in Groups of Workers as an Index of Inorganic Lead Absorption.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 58-62, 3 figs. [13 refs.]

The determination of the average Donath coproporphyrin scale reading in lead processing industries in the Netherlands—a quick screening procedure possible on factory premises—is shown to give an approximate estimation of the degree of atmospheric Pb concentration and of anaemia. If in a group of at least 20 workers the reading is 1.5 degrees, coproporphyrinuria values are within normal limits and no danger of manifest Pb intoxication exists. If it exceeds the allowable range of 1.5-2.5 degrees, which corresponds to approximately 0.1 mgm. Pb per m³, individual stippled counts and haemoglobin estimations are necessary.

In this semi-quantitative test, 10 ml. urine are shaken in a test tube with 2 ml. ether-glacial acetic acid, and the fluorescence of the foamy ether layer in ultra-violet light is compared with that of standards which are 8 prepared paper circles on a rotating disc. Degrees Nos. 1-7 of this scale were used, corresponding respectively to the following 7 increasing coproporphyrin concentrations expressed as μ gm. per litre:—0-50; 50-100; 100-200; 200-400; 400-800; 800-1,600; and more than 1,600. In 112 men, not exposed to Pb, degrees 1, 2 and 3 were found respectively in 70%, 20% and 10%, the "normal" average reading being 1.4 degrees. Investigations were carried out in 513 men exposed to Pb.

In 2 factories groups exposed to less than 0.05 mgm. Pb per m³, had mean readings of less than 3 degrees; with more than 0.15 mgm. readings were more than 3 degrees and they increased with increasing concentrations but not with duration of exposure. Ranges varied and there were a few exceptions. Among non-exposed

workers haemoglobin values less than normal were found in 25%. Among exposed workers more than 25% had anaemia where average readings exceeded 2·2·5 degrees, and the correlation between the percentage with low haemoglobin and high-scale readings was high in 16 groups of printers, painters, etc. [see ZIELHUIS, this *Bulletin*, 1961, v. 36, 239; KING and THOMPSON, *ibid.*, 333; DONATH, *Archiv. Hig. Rada*, Zagreb, 1956, v. 7, 77.] *M. Patricia Fitzsimons*

CHERCHI, P. & SPINAZZOLA, A. Sul comportamento delle prove omogeniche in soggetti esposti al rischio saturnino. [Study of the Coagulability of the Blood and Capillary Resistance in Persons Exposed to Lead] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Dec., v. 41, No. 12, 655-62. [13 refs.]

The literature on the coagulability of the blood and of capillary resistance in lead intoxication is first reviewed but only a few references were found, and those almost entirely by Italian authors.

28 subjects were studied, most of them workers in a lead foundry but a few were employed in the printing industry. They were divided into 3 groups: in the first (numbering 14 cases) were placed all those subjects with clinical and biological signs of chronic lead intoxication: there were 7 in the second group which consisted of those without obvious clinical evidence of lead poisoning but with clear biological signs of absorption of the metal; in the third group were put those 7 subjects who had no clinical or biological signs of lead intoxication but had been exposed to risk for a long time (10 to 30 years). In addition to the investigations necessary to establish the existence of lead intoxication the following haematological tests were undertaken:—tourniquet test, Hecht's test, bleeding time, coagulation time, Howell's recalcification time, platelet counts, clot retraction, Quick test, fibrinogen level.

The protocols of all the 28 subjects investigated are presented in a table giving the results of the tests in detail. More than half the workers with clinical signs of lead intoxication, and a third of those with signs of increased lead absorption, gave results in the tourniquet and Hecht tests, 10-15% above the normal level. The changes in fragility of the blood vessels are generally proportional to the degree of absorption of the metal and to the duration of exposure to risk.

Confirmation of the observations made by the authors has been obtained by other workers showing that prothrombin activity is lessened in persons with signs of chronic lead intoxication and that this is also true to a large extent in workers showing evidence of increased absorption of the metal.

G. F. Keatinge

IORANIDIS, P. Étude comparative de l'hématie ponctuée, du sidérocyte et du réticulocyte dans le saturnisme expérimental. [A Comparative Study of the Punctate Red Cell, Siderocyte and Reticulocyte in Experimental Lead Poisoning] *Arch. Malad. Professionnelles*. Paris, 1960, Dec., v. 21, No. 12, 719-26, 4 diagrams. [56 refs.]

A diagram and graphs show the times at which these cells appear in and disappear from blood and marrow in 19 rabbits after Pb poisoning. Characteristics, evolution and numbers are described, and staining methods evaluated. A 0·5% solution of Pb acetate, 1 mgm. per 100 gm. body weight, was injected intraperitoneally every 2 days until punctate red cells exceeded a count of 100 per 100 white cells—white cells in France being the legal standard in such counts. Then a double dose was injected twice weekly until the count was doubled. Blood and iliac crest marrow samples were taken beforehand and from 3 days after the first injection until punctate cells appeared and then every 3 days until 3 negative smears were obtained.

First to appear, in 3 days, were punctate cells in marrow and, except reticulocytes, they lasted the longest, for 142 days. Erythroblasts with basophil granulations followed a similar course. Next, in 5 days, reticulocytes appeared in marrow, and in 6 days in blood, whence respectively they disappeared in 149 and 146 days. In 8 days punctate cells appeared in the blood, they went on increasing for approximately more than 1 month after the last injection and disappeared 124 days later (range 95-138). Until they reached 800 per 10⁵ red cells the punctate cells were outnumbered by reticulocytes but then the increase in the latter slowed. Punctate cells reached a maximum of 1,400 per 100 white cells, mean 613. Siderocytes in marrow appeared in 16 days and went in 118, and sideroblasts seemed less numerous with Perls stain than with Turnbull blue. Siderocytes in blood were seen from 19 to 112 days, disappearing and reappearing sporadically. There was no correlation between them and punctate cells, nor between variations in the number of the latter and those of reticulocytes. No Heinz bodies were observed.

M. Patricia Fitzsimons

DHAR, D. C. The Influence of Adrenal Cortex on Lead Anaemia and the Effect of ACTH and Cortisone. *Indian J. Med. Res.* 1961, Jan., v. 49, No. 1, 33-41, 5 graphs. [20 refs.]

Adrenalectomized rats were used in some of these experiments, undertaken to evaluate effects of hormone therapy on anaemia induced by lead, since encouraging results had been reported when some varieties of anaemia had been treated with cortisone and ACTH. Poisoning was induced by intravenous injection of a solution of Pb acetate, 6 mgm. per 100 gm. body weight. After operation 1% saline was substituted for drinking water. A table gives serial haemoglobin levels and red cell counts for 14 days in most of the groups and in anaemic controls which were intact, untreated rats poisoned with Pb. Percentage changes in values shown by experimental groups are plotted against those of controls.

Pretreatment with cortisone intramuscularly, 20 mgm. per 150 gm. rat, or with 5 mgm. corticotrophin subcutaneously, was given to 2 groups 3 hours before poisoning and to 2 others before adrenalectomy and poisoning. Other intact rats 6 days after poisoning were treated for 5 days with 5 mgm. cortisone or 2 mgm. corticotrophin.

Intact rats showed an improvement in Pb anaemia from cortisone or corticotrophin in the single or repeated

doses, corticotrophin being more effective. Rats which were poisoned after adrenalectomy died in 1 day but adrenalectomized control rats which were injected with 0.2 ml. water per 100 gm. survived and did not develop anaemia. Poisoned adrenalectomized rats pretreated with corticotrophin died within 2 days but those pretreated with cortisone survived. These developed anaemia more quickly and severely than intact animals, but it improved. After discussion it is concluded that in Pb anaemia the adrenal cortex has some direct role in blood formation and that corticotrophin and cortisone increased the production of erythrocytes and haemoglobin.

M. Patricia Fitzsimons

CAFRUNY, E. J. **A Rapid Procedure for Determination of Mercury in Urine and Kidney.** *J. Lab. & Clin. Med.* 1961, Mar., v. 57, No. 3, 468-72, 1 fig.

"A rapid and simple procedure for the determination of mercury in urine and kidney tissue is described. Potassium bromide is used to liberate mercuric ion from organic complexes and renders unnecessary any of the laborious manipulations usually employed in preparing samples for analysis. Free mercuric ion is then extracted in chloroform solutions of dithizone. The colored mercury dithizonate complex formed can be determined spectrophotometrically. Results using this method are equivalent to those obtained with a polarographic procedure. Renal and urinary mercury concentrations after administration of therapeutic doses to rats and dogs are comparable to those reported in the literature. The method may be used to study excretion of mercury in patients treated or poisoned with organic mercurial diuretics or inorganic mercury. As little as 10 mcg. mercury per milliliter of urine may be detected but, with minor changes, sensitivity can be adjusted for measurement of 1 mcg. mercury."

SMITH, A. D. M. & MILLER, J. W. **Treatment of Inorganic Mercury Poisoning with N-Acetyl-D, L-Penicillamine.** *Lancet.* 1961, Mar. 25, 640-42, 1 fig. [10 refs.]

Rapid recovery followed treatment with this chelating agent which is therefore advocated for further trial in mercurialism. After 15 years' work in a London factory where his predecessor had died from mercury poisoning with nephrosis and uraemia, a hand-gilder, aged 56, developed classical chronic mercury poisoning when the articles to be gilded increased in number and size because of orders from new African States for various state insignia. The gilding was done twice each week by possibly the only hand-gilder in Britain. Exhaust from his charcoal fire was inadequate; the paste-like mercury-gold amalgam was handled and applied to the article which was heated and repeatedly brushed. [The description of the process is classical in itself, and so is the reproduction of handwriting from the working diary; the legibility after treatment is striking.]

Gross intention tremor of the hands for 3 months before admission did not result in the patient's giving up

work, but did result in his breaking most of the household crockery. He was only slightly irritable. There was milder tremor of head and eyebrows and ataxia; dysphonia was demonstrated to be due to jerky vocal cord movement. Slit-lamp examination showed blue-grey mottling of the cornea and polychromatic lustre of the post-lens capsule. Electroencephalograms showed a mild paroxysmal instability only, retained after treatment. All other investigations, including chromatography of urine for amino acids, were normal, except urinary excretion of Hg. This before treatment was 1,369 μgm . daily and during three 10-day courses of treatment, at 17-19-day intervals, it became:—1,828 and 1,639; 600 and 420; and finally 290 μgm . The dose of N-acetyl-D,L-penicillamine was 250 mgm. 4 times daily. Improvement after the 2nd course permitted discharge, and there was almost complete recovery 1 month later.

M. Patricia Fitzsimons

AMANTE, L., MAGISTRETTI, M. & PERNIS, B. **The Action of Arsenic on Reduced Glutathione.** *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 11-13, 2 figs.

"We have shown that haemolysis induced by arsenic is related to a fall in reduced glutathione (GSH) in the erythrocytes concerned, the GSH being converted into oxidized glutathione (GSSG). This reaction requires the presence of O_2 and shows no stoichiometric relation between arsenic concentration and the amount of GSH which disappears from the erythrocytes. The present work establishes that it is possible to restore the initial concentration of GSH, after its disappearance, induced by arsenic, by means of electrolytic reduction. This observation permits us to state that the action of arsenic on erythrocyte GSH is not based on the formation of a compound of arsenic and GSH, but rather arsenic or one of its oxidation products (e.g. elementary As) acts catalytically, on the reversible conversion of GSH into GSSG."

KAPLUN, Z. S. & MEZENCEWA, N. W. **Experimental-studie über die toxische Wirkung von Staub bei der Erzeugung von Sintermetallen. [Experimental Study of the Toxic Action of Dust in the Production of Sinter-(hard-) metals]** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 390-99, 1 fig. [22 refs.]

Hard metals or sinter metals are made from a mixture of tungsten and titanium carbides amalgamated with cobalt. In the process of manufacturing these metals the most dusty processes are the mixing of the metallic tungsten with carbon, the heating and sieving of cobalt oxide, and the sieving, granulating and grinding of the mixture of metals. From the periodical examinations of 283 workers in these dusty places it was found that those who came into contact only with tungsten and its combinations showed slight changes in the respiratory organs. Workers exposed to mixtures of tungsten and cobalt complained of poor appetite, cough, and the loss of the sense of smell. Many had also low blood pressure and changes in the blood.

This paper gives the results of several series of experiments on white rats to ascertain the effects of the individual constituents of the dust. In the first place tungsten carbide, metallic tungsten, tungsten oxide and titanium carbide were used. Animals were exposed to these dusts either in a dust chamber or by intratracheal injection. All the dusts produced in the lungs a proliferation of lymphoid-histiocytic elements round the bronchi and larger vessels; with longer exposures, small collagenous fibres were found in the peribroncheal and perivascular tissue. Tungsten oxide gave the most distinct changes. In contrast to titanium carbide, tungsten and its compounds affected the walls of the smaller vessels.

A separate experiment was made with metallic cobalt. Very definite changes were found in the blood vessels, and the walls of the bronchi showed inflammatory changes. Small rounded glandular formations were present in most of the rats. With suitable staining, fine connective tissue fibres were demonstrated in the tissue round the small and medium bronchi and blood vessels. Physiological investigation showed hypotension, changes in the blood, as well as functional damage to the nervous system demonstrated by chronaxie studies. Experiments with cobalt oxide showed that it had no distinct general action but it could produce more pronounced changes in the lungs than metallic cobalt.

Mixtures of tungsten, titanium and cobalt were then studied. Cobalt had already been shown to have the highest toxicity, and this was increased in the mixtures. The chronic changes found in the places where the dust accumulated were thickening of the parenchyma of the lung caused by increase of the lymphoid cells, histiocytes and fibroblasts. Round the medium and small bronchi these accumulations were massive. The mucous membrane of the bronchi was hypertrophied, forming tumours and adenoma-like structures. These changes are similar to those caused by cobalt but are much more advanced.

Tests of the solubility of cobalt in a solution of hydrochloric acid of pH similar to that of gastric juice indicated that the presence of tungsten dust increased its solubility. This is given as the cause of the increased effect of cobalt in mixtures with tungsten.

Charles L. Sutherland

NOWACKI, J. Doświadczalne ostre zatrucia tlenkiem kadmu u białych szczurów. [Experimental Acute Poisoning by Cadmium Oxide in White Rats] *Med. Pracy.* 1961, v. 12, No. 1, 27-30, 1 fig.

The English summary appended to the paper is as follows:—

"5 white rats were submitted in an experimental chamber to the action of dust of the alkaline accumulators negative mass. The cadmium oxide is a chief constituent of this mass (57—63 p. c.). The cadmium concentration in the chamber amounted to about 100 mg./c.m. of air; the experiment lasted for 2 hours. Three rats were dead on the very day of exposure, the remaining two after 6 and 11 days.

"It was stated that the balance disturbances were the chief phenomenon of the intoxication of animals. After the death of animals the cadmium content in some internal organs was examined. It was stated that its

content in the liver was 0.09 p. c., in the stomach 0.05 p. c., in kidneys, heart and spleen 0.001 p. c., in brain 0.005 p. c., calculated in grams of dry residue after incineration of the organs.

"The author comes to the conclusion that the danger of intoxication depends to a great extent on the size of dispersion of cadmium particles in the air."

CAMERA, V. Metodo colorimetrico per la determinazione di microquantità di uranio in materiali organici e inorganici mediante 1-(2-piridilazo)-2-naftolo (PAN). [PAN (1-(2-Pyridilazo)-2-Naphthol) Colorimetric Micro-Method for the estimation of Uranium in Organic and Inorganic Materials] *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 59-69, 3 figs. English summary.

YAMADA, S.; MATSUSHITA, T.; ISHIKAWA, Y. [Effect of Cyclohexan, as a Less Toxic Substitute for Benzol, on the Blood Pictures. (1) An Investigation in a Polyethylene Printing Shop] [YAMADA, MATSUSHITA & ISHIKAWA]. *J. Sci. of Labour.* Tokyo. 1960, Oct., v. 36, No. 10, 546-52, 3 figs. [14 refs.] [In Japanese] English summary. [(2) An Experimental Study in Rats] [YAMADA]. *Ibid.*, Nov., No. 11, 598-603, 5 figs. [14 refs.]

1. Benzol poisoning was observed in Japan during 1957-59, especially in home workers and workers in small plants [the type of work is not explicitly stated in the English summary]. Cyclohexane was substituted for benzol as a solvent, in a polyethylene sheet printing shop, and whereas with benzol the workers had shown anaemia, leucopenia and a high rate of Mommensen's toxic granules in the leucocytes, after they had used cyclohexane for a month these features had lessened, and after 6 months, during part of which anti-anaemic treatment was given, the blood picture was normal.

2. The author performed experiments on rats to compare the effect of benzol injected daily in olive oil, with cyclohexane similarly administered. The results confirmed the former finding that cyclohexane was less toxic than benzol, though its toxicity was not negligible. Both substances in relatively large doses inhibited mitosis of myeloid cells and erythroblasts in bone marrow, but cyclohexane less than benzol.

Some details of dosage are given in the English summary.

Charles Wilcocks

BÄNFER, W. Untersuchungen über Einwirkung von Reintoluol auf das Blutbild von Druckern und Hilfsarbeitern im Tiefdruck. [Investigation of the Effect of Pure Toluene on the Blood Picture of Rotogravure Printers and Auxiliary Workers] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1961, Feb., v. 11, No. 2, 35-40, 3 figs. [21 refs.]

Benzene, toluene and xylene have been widely used in colour printing on account of their speed of evaporation and good solvent capacity, but benzene, the best technically in these respects, has, owing to its haemotoxic

action, been generally replaced by toluene and xylene. Commercial toluene and xylene contain a certain amount of benzene (up to 15% for toluene) but pure preparations of both are now available.

Animal experiments have shown that chronic exposure to toluene and xylene is much less harmful than to benzene, but it has only recently been suspected that the reason lies in the difference in their intermediary metabolism. Benzene is converted to phenols (protoplasmic poisons), catechols and hydroquinone; these are to some extent detoxicated by conversion to sulphuric and glucuronic acids, which are excreted. Toluene, by oxidation of its methyl group, is converted to benzoic acid, synthesizes with glycocholic acid and is excreted partly as hippuric acid and partly as benzoyl glucuronic acid. Xylene is excreted as toluic acid.

The present investigation on toluene containing only 0.3% of benzene, as ascertained by chemical analysis, included blood examinations of a large number of workers employed for more than three years in rotogravure printing. They were carried out every 3 months in young persons under 18, every 6 months in adults, and included enumerations of erythrocytes, total leucocytes, polymorphonuclear leucocytes, and estimation of haemoglobin.

Analysis of the air of the workroom revealed no benzene or xylene. In 3 samples the toluene content was less than the MAC, in one equal to it and in one reached 400 p.p.m.

Results of blood examinations showed that only 3 times in all was the total white count less than 4,000, the polymorphs were never lower than 2,000, and there was no absolute or relative lymphocytosis. The red cells and haemoglobin showed only slight occasional variations. Sternal puncture of 5 workers with a total white count of less than 5,000 showed no pathological changes.

Comparison with control workers having at the time no contact with toluene showed a very similar blood picture, the only difference being a higher proportion of the controls having a total white count exceeding 8,500.

It is concluded that though it is not possible, without a much longer and more exact investigation, to state categorically that pure toluene cannot have any injurious effect on the haemopoietic system, it has certainly a much less toxic effect than benzene.

Ethel Browning

MACKIE, I. J. Methyl Chloride Intoxication. *Med. J. Australia*. 1961, Feb. 11, v. 1, No. 6, 203-5. [10 refs.]

An unusual case of methyl chloride intoxication would very likely have been fatal had it not been for the administration of adrenal steroids. The patient, aged 40, had worked in his refrigerating plant for 18 years with methyl chloride which, he complained, had been marked "Non-Toxic". For 6 months exposure had been heavy and, after good health except for recent impotence, during this time he became weak, thin and pale. He developed pyrexia, vomiting, muscle pains and jaundice; the urine was dark and faeces pale. Transient erythema, revulsion for alcohol and smoking, headache, thirst and polyuria

preceded admission to hospital 6 weeks after the jaundice started. Tachycardia, deep jaundice, profound pallor and enlargement of liver and spleen were noted. The urine contained protein, bile pigments and salts and no abnormal metals. The blood contained 3.2 gm. haemoglobin per 100 ml.; the white cell count was raised with a leukaemoid response; blood urea was raised; Schumm's test and liver function tests were positive. Tests for hydatid disease, syphilis and malaria were negative. Liver biopsy 1 month later showed necrosis with regeneration, mainly in the centre of the lobules, and early reticuline formation, and 4 months later was normal. By this time, the only abnormality was a palpable liver. The patient was strong and well, though still taking a reduced dose of prednisone. Improvement had begun after this was given 2 days after admission when even slow transfusion of packed red cells rendered digitalization necessary.

This case of liver damage, kidney damage and acute haemolysis—which have been reported in some of the 200 cases of methyl chloride poisoning in the literature—did not follow the general clinical pattern believed to be due to metabolism to methyl alcohol and formaldehyde, though blurred vision was noted.

M. Patricia Fitzsimons

GAULTIER, M., FOURNIER, E., GERVAIS, P., GORCEIX, A. & EFTHYMIU, T. Deux observations d'intoxication par le sulfate de méthyle. [Two Case-Notes of Poisoning by Methyl Sulphate] *Arch. Malad. Professionnelles*. Paris. 1960, Dec., v. 21, No. 12, 744-6.

Post-mortem analysis in one of these cases showed that the blood contained 0.17 gm. ethanol, and 0.052 gm. methanol, per litre; the viscera contained 0.4 and 0.06 gm. per kgm. respectively, and 0.01 gm. acetaldehyde, and 0.375 gm. sulphates, per kgm. Though the post-mortem findings of purulent bronchitis, pulmonary congestion, atheroma and slight fatty degeneration of the liver were attributed to natural causes, it was concluded that the methanol found was consistent with hydrolysis of dimethyl sulphate from accidental exposure 12 hours before death. The blood sulphate was normal (0.75 gm. per kgm. in text) but the viscera contained more than generally found. This was the case of a man aged 69 with a past history of bronchial trouble, who became ill 5 hours after a 10-litre carboy of dimethyl sulphate was broken, with escape of 50-100 ml. He washed his skin but did not remove towels from the workroom and refused to stop work. Clothing was not splashed. He was admitted to hospital 8 hours after the accident. His companion, aged 72, was admitted at the same time, having developed, as usual some hours after exposure to this irritant, symptoms of eye, nose, larynx and lung irritation. This man's course, investigations and treatment are described. He recovered a month later.

The toxic effects outlined and the MAC of 1 p.p.m. give emphasis to precautionary measures which especially in laboratories are necessary. Apparatus and equipment should be free of faults. Workers should be trained to leave the area if dimethyl sulphate escapes. Splashed clothing should be removed. An exposed person, after

eye lavage, should be removed by ambulance, and bed rest for 3 days enforced. The difficult problem of treating pulmonary oedema in the presence of hypertension is discussed and also the question of assisted respiration.

M. Patricia Fitzsimons

SPIOCH, F. M. & HRYCKO-SPIOCHOWA, Maria. Działanie cytochromu *C* w doświadczalnej hipoksji wywołanej zatruciem tlenkiem węgla. [The Effect of Cytochrome *C* in Experimental Hypoxia induced by Carbon Monoxide Poisoning] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 4, 759-74, 7 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"The effect of cytochrome *C* on the oxygen utilization by normal tissues and those taken from animals with lethal CO poisoning was studied manometrically in Warburg's apparatus. Cytochrome *C* was found to exert no action on oxygen consumption by normal tissues. The encephalon, myocardium and liver of the lethally poisoned animals showed a marked decrease in oxygen consumption, the level of their carboxyhemoglobin amounting on the average to 80%. The addition of cytochrome resulted in a considerable oxygen utilization in all three organs under investigation. Histopathologic studies of sections from the encephalon, myocardium and liver of poisoned animals showed changes corresponding with circulatory disturbances and degenerative lesions. No correlation could be established between the intensity of histopathologic changes and the reduction in oxygen consumption, the latter being a reversible phenomenon, brought about by the inhibition of the respiratory system. On the other hand, it has been found that the organs showing the slightest histopathologic changes (myocardium) exhibited the highest increase in the oxygen utilization following the addition of cytochrome *C*. As a result of poisoning-conditioned oxygen debt, the oxygen consumption under the effect of cytochrome exceeded that of normal organ sections.

"When animals were being poisoned for 30 and 80 minutes at first an increased oxygen consumption was found, followed 10-15 minutes later by a sudden fall to 1/3 of normal values, which persisted to the completion of the experimental phase. The HbCO level at the end of the intoxication experiment was on the average 70%. In the phase of detoxication, a sudden increase in oxygen utilization beyond the normal values occurred after 20 minutes to return to normal level after 2 hours. Intracardiac administration of cytochrome *C* ('Cyto-Mack' and 'Biosedra') was found to affect neither oxygen utilization rate nor its total uptake. The increase in oxygen consumption by poisoned organ sections due to the effect of cytochrome *C* was not in keeping with oxygen uptake increase in animals *in toto*. The HbCO of the order of 30% did not affect the oxygen utilization pattern both of animals which received cytochrome and of those which were given NaCl. The HbCO level seems to be significant in poisoning only within certain limits and may be an evidence of its severity. The lack of cytochrome *C* effect on the oxygen uptake in animals under investigation may be explained as follows: a) the introduction of cytochrome into the circulation delays

or interferes with its access to the cells as compared with studies on organ section; b) the rate of changes occurring in the organism is so high that the normal oxygen utilization and compensation of temporary under-oxygenation are accomplished before the action of cytochrome is displayed; c) lethal poisoning of animals from which the sections were taken for examination, lasted on average 3 hours, whereas the experimental poisoning was performed within 30 or 80 minutes.

"The authors discussed the effect of cytochrome on the poisoned organs, the inhibitory action of carbon monoxide on the respiratory cell system *in vivo* in connection with Warburg's studies, as well as the reasons responsible for the disparity in results obtained with organ sections and animals *in toto*. Further studies on the mechanism of CO poisoning and cytochrome action combined with other pharmacologic substances are in progress."

GIRAULT. Action du carbonate de soude chez les ouvriers emballeurs. [The Effect of Sodium Carbonate on Packers] *Arch. Malad. Professionnelles*. Paris. 1960, Dec., v. 21, No. 12, 747-50.

Since preventive measures were taken 12 years ago there have been no further cases of nasal perforation in this soda packing factory. After complaints of nose bleeding 21 perforations were found among 160 employees, mainly among dockers and packers, especially among those handling powdered soda. Periodic examination showed that congestion of the nasal mucosa was followed by ulceration and perforation sometimes accompanied by total cartilage destruction. Friction lesions of the skin, caused by the rough fibres of sisal sacks, were common, and the combination of sweat and soda caused ulcers similar to the brine holes of salt workers. Soda holes were mostly on hands and wrists, though the dockers, who carried the sacks in their arms and not on the shoulders, had them on the trunk and arms. Those with fair skin were more prone. Eczematous dermatitis affected a few workers who handled crystals as well as a few exposed to powder. No other effects were found on bronchoscopy or annual X-ray examinations of the chest. The incidence of pulmonary tuberculosis, 5 in 15 years, was less than among a comparable number in the factory not exposed to soda.

Some powder collected around the filling machines, but the greatest danger was from the powder which escaped through the wide mesh of sisal sacks on to conveyor belts, runways, waggons and barges. This was overcome by the use of jute sacks, and paper containers were best. In 1946 nasal douching followed by the application of a haemostatic salve to the nostrils, before and after work, was started. Bleeding and ulceration have been cured by this treatment.

M. Patricia Fitzsimons

DUTKIEWICZ, T. Wchłanianie par aniliny u ludzi. [Aniline Vapours Absorption in Men] *Med. Pracy*. 1961, v. 12, No. 1-14, 7 figs. [41 refs.]

The English summary appended to the paper is as follows:—

"The absorption of aniline vapours through the skin (23 experiments) and in the respiratory tract (8 experiments) were studied in humans. For this purpose a toxicological chamber was applied, where desired constant conditions (aniline vapours concentrations, air temperature and humidity) were obtained. In all experiments the p-aminophenol excretion in urine was examined.

"The aniline vapours retention in lungs was constant and equal in several subjects (about 90 p. c.).

"The absorption velocity of aniline vapours in the respiratory tract in concentrations of 5–30 $\mu\text{g/l}$ ranges from 2 to 11 $\mu\text{g/h}$, when the mean value of inhaled air is 418 l/h.

"The absorption velocity of aniline vapours through the skin in a completely naked, resting person, in the temperature 25°C and the humidity 35 p. c., in concentration 5–50 $\mu\text{g/l}$, ranges from 3 to 11 mg/h. This absorption velocity increases according to the temperature and humidity of the air. The use of a simple overall decreases the absorption velocity by 40 p. c.

"A close dependence was stated between the dose of aniline absorbed in the lungs and the excretion of p-aminophenol in urine (measured as excretion velocity in the time between the 6th and the 8th hour from the beginning of the exposure, or the amount of p-aminophenol excreted in 24 hours urine).

"This dependence is in very good conformity with the analogical dependence stated previously when studying the liquid aniline absorption through the skin. In two factories applying aniline in the production process, the routes of absorption have been studied. It was found that in the existing conditions about 75 p. c. of the absorbed aniline amount got in the body through the skin."

GRYBOSKI, Joyce, WEINSTEIN, D. & ORDWAY, N. K.

Toxic Encephalopathy apparently related to the Use of an Insect Repellent. *New England J. of Med.* 1961, Feb. 9, v. 264, No. 6, 289–91.

A previously healthy well-developed child age 3½ years rapidly became ill with repeated "Shaking and crying spells" lasting 2 minutes and recovering every 5–10 minutes. The child was confused. No abnormalities of blood, urine or cerebrospinal fluid were detected. Bacterial and viral cultures were negative. The attacks were controlled by sodium amylal and after 2 days treatment they did not recur and the child made a complete recovery. The authors cautiously concluded that the condition must have been due to poisoning by an insect repellent containing 15% of N-N-diethyl-m-toluamide in denatured alcohol with a Freon repellent. A total volume of 180 ml. had been sprayed on the child's bedding every night for 2 weeks before the illness. N-N-diethyl-m-toluamide causes convulsions in rats but only in doses of 2 ml. per kgm. body weight.

[Published work on N-N-diethyl-m-toluamide (AMBROSE, 1959, *Toxicol. & Applied Pharmacol.*, 1959, v. 1, 97) included observations in which men had had the repellent applied repeatedly to their skin. The only adverse reaction was some mild irritation.]

J. M. Barnes

ROCHE, L., LEJEUNE, E., MADONNA, ROBERT, J. M. & LACHËZE-REY. A propos de 4 observations d'intoxication par le Phosphène. [Poisonings by the Insecticide—Phosphène (syn. Phosdrin; Carbomethoxymethylvinyl dimethyl Phosphate)] *Arch. Malad. Professionnelles.* Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 52–5.

Here presented are 4 case reports of poisoning in workers exposed to the organic phosphorus compound "Phosphène" [Phosdrin] which is being used as a general insecticide in market gardens. All the patients recovered in a few days having been treated mainly by the administration of atropine.

The main symptoms among these patients were:—faintness, fainting fits, giddiness, misty vision, pronounced sweating, nausea, vomiting, diarrhoea and shortness of breath with pains in the chest in 1 or 2 instances. Some of these symptoms began either during work or 1–2 days after exposure.

Signs noted were pallor, cold extremities, moderate bradycardia and miosis (in 1 or 2 cases). In all patients it was noted that the breath had a marked aroma of phosphorus. Particulars of the blood examinations are given and cholinesterase estimations carried out in 3 of the 4 cases showed a considerable diminution in concentration.

It is recommended that Phosdrin and other organic phosphorus insecticides which are not at present recognized by the law concerning industrial illness should be included in the official list for purposes of compensation.

M. E. Delafield

GAULTIER, M., FOURNIER, E., GERVAIS, P. & GORCEIX, A.

Traitement par le 76-76 RP (N-Méthyl- α -pyridyl-aldoxime) d'une intoxication grave par un insecticide organo-phosphoré (parathion). [Treatment of Severe Parathion Poisoning with 76-76 RP (N-Methyl- α -Pyridyl-Aldoxime)] *Arch. Malad. Professionnelles.* Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 55–7.

The authors describe the treatment of a severe case of parathion poisoning at the poisons centre of the Fernand Widal hospital.

The patient was a boy of 17 years who had swallowed about 0.8 gm. of parathion in an attempt at suicide. This produced severe symptoms leading to coma and convulsions. His early treatment consisted in atropine (4.25 mgm. in the first 3 hours) and gastric lavage. After about 3 hours he had severe pulmonary oedema and this was treated by the removal of 300 ml. blood and the injection of camphor and coramine subcutaneously and chlorpromazine intramuscularly. His cyanosis became worse and this was treated by intubation and then tracheotomy with oxygen and artificial respiration, although the cyanosis was removed the coma and convulsions persisted. 7 hours after poisoning he was given 1.0 gm. N-methyl- α -pyridyl aldoxime (76-76 RP) intravenously. This had a dramatic effect, for 20 minutes after the infusion of this compound had begun the convulsions

ceased and he came out of coma. A further dose of 200 mgm. was given 10 hours later and after 2 days he had

completely recovered. The authors discuss the implications of this case.
H. B. Stoner

HEATING, LIGHTING AND VENTILATION

HINCHCLIFFE, R. **Some Aspects of Nasal Function and Dysfunction in relation to Environmental Air.** *Ann. Occup. Hyg.* London. 1961, Jan., v. 3, No. 1, 6-21, 1 fig. on pl. [Numerous refs.]

This paper was delivered at a joint meeting of the British Occupational Hygiene Society and the Ergonomics Research Society held in London on 24 June, 1960. As the audience included non-medical scientists the author before expounding his theme gave a very excellent account of current knowledge of the anatomy and physiology of the nose and paranasal sinuses. In the course of this he cited extensively the work of experts in these fields of study. He then reviewed the present state of knowledge of nasal dysfunctions related to environmental air conditions. The methods of investigating nose-environmental air relationship were discussed under 3 main headings: (1) Animal experiments, (2) Human physiological experiments; the climatic room, and (3) Epidemiological investigations: (a) in respect of air conditioning, and (b) in respect of different climatic areas [geographical]. It is concluded that "the precise importance of environmental air conditions in the pathogenesis of nasal dysfunction and their influence on the prevalence of nasal disease has yet to be elucidated. Available evidence, however, indicates that artificial climates, in the sense of air-conditioning of offices or factories, do not influence the prevalence or attack rate of upper respiratory or other diseases.

"It would seem that further enquiries into the relationship between nasal dysfunction and environmental air conditions must primarily take the form of epidemiological investigations. Feasibility studies that we have conducted indicate that such investigations are possible using radiographic methods."

For future surveys in this field the author stresses the value of the epidemiological method and he favours "the respiratory tract" rather than the "E.N.T." approach. This signifies that "sinusitis" investigations should be combined with "bronchitis" surveys [this *Bulletin*, 1958, v. 33, 238; 1959, v. 34, 238].

A. Meiklejohn

YAGLOU, C. P. **Limits for Cold, Heat and Humidity in Underground Shelters.** *Arch. Environment. Health.* Chicago. 1961, Feb., v. 2, No. 2, 110-15, 1 fig.

In this paper the minimal thermal standards for radiation fall-out shelters, where people may have to remain for 2 weeks, are considered. The limits are expressed in terms of effective temperature.

Acceptable and tolerable thermal limits for healthy people at rest and "properly clothed" [presumably "suitably clothed"] are given as:—

	Effective temperature, °F.
Lowest temperature endurable in cold weather for at least two weeks in emergencies ...	35
Possible chilblain or shelter-foot ...	35-50
Lowest acceptable for continuous exposure, manual dexterity may be affected ...	50
Optimum for comfort, with 60% relative humidity ...	68-72
Perspiration threshold. Acceptable for continuous exposure ...	78
Endurable in emergencies for at least two weeks, possible heat rash in prolonged exposures ...	85
Possible heat exhaustion in unacclimatized people ...	88
Possible heat exhaustion in acclimatized people	92

Predictions are made of the extremes of heat and humidity likely to develop in underground shelters, and from these it is concluded that underground fall-out shelters can be designed to maintain thermal conditions in temperate or arctic regions that will be acceptable for isolation periods of about 2 weeks, with little or no artificial heating or cooling, and with only minimal ventilation. In desert regions, and in many hot and humid areas, where soil temperatures at shelter depth are of the order of 75° to 85°F., mechanical cooling of shelters will be essential.

Thomas Bedford

Food and Nutrition

The order in this section is:—General; Foodstuffs; Food Poisoning.

FOODSTUFFS

(Composition and Bacteriological Control)

(i) MINISTRY OF HEALTH: MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **Hygiene in the Retail Fish Trade.** *Food Hygiene Codes of Practice No. 3.* 18 pp., 1 fig. 1960. London: H.M. Stationery Office. [9d.]

(ii) MINISTRY OF HEALTH: MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **The Hygienic Transport and Handling of Fish.** *Food Hygiene Codes of Practice No. 4.* 15 pp., 2 figs. 1960. London: H.M. Stationery Office. [9d.]

These codes of practice are issued jointly by the Ministries of Health, and Agriculture, Fisheries and Food, and in his introductory letter the Minister of Health points out that they give advice and guidance which the Food Hygiene Regulations (1960, No. 1601) cannot.

(i) This code is divided into various sections dealing with structure, fittings, equipment, storage and sale, and matters relating to staff including cleanliness, protective clothing, etc.

In general there is little to take exception to though as regards staff too much emphasis is laid on the need for keeping finger-nails short when dealing with fish products, thus giving the impression that this is not so important when dealing with fish in other ways. It is axiomatic that nails must be kept short when handling any kind of food whether raw or processed in any way at all. As regards protective clothing the point should have been made that it is not enough that this can be easily washed but that this must be done frequently, and there is no mention of the use of plastic materials. Unfortunately it is nowhere pointed out in the code that the owner or occupier of the premises and the staff have certain duties under the regulations with which they must as against *should*, conform. In fact many points in the code are covered much better in the regulations.

(ii) This code is again divided into a number of sections and is a very sound exposition of good practice. There is an excellent summary of the advantages and disadvantages of the various kinds of fish containers or boxes. More emphasis could perhaps have been placed in paragraph 42 on the necessity of separating fish from game in fur or feather. The great importance of handling fish carefully is well emphasized.

[The demand for frozen fillets, etc., is an indication that the public taste in fish is changing rapidly and changes are evident in problems affecting the distant water fleets and the inshore fishermen. All of these will have repercussions on the trade and the Codes will have to keep up to date with them. A point which might very well have been made by the Minister of Health in his letter is that local Medical Officers of Health and Public

Health Inspectors are very willing to give advice if asked.]
W. K. Dunscombe

DIXON, J. M. S. & POOLEY, F. E. **Salmonellae in a Poultry-Processing Plant.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, Feb., v. 20, 30–33.

The investigation was carried out in a factory processing and packing 12,000 12-week-old broiler chicks daily.

Specimens were taken at weekly intervals for 23 weeks and included samples of water from 2 “chilling” (4°C.) tanks and from “scalding” tanks (53° or 60°C.), swabs suspended in the chilling tanks for 6 hours and swabs from eviscerated carcasses and from edible viscera.

13.8% of 544 specimens were positive for salmonellae on 13 of 23 weekly visits. Positive samples included 21 of 87 samples of water and 19 of 60 swabs immersed in chill tanks, 30 of 297 swabs from eviscerated carcasses, 3 of 37 swabs from edible viscera, and 2 of 22 swabs from staff members.

9.9% of the eviscerated carcasses and edible viscera harboured salmonellae. *Salm. typhi-murium* was isolated from 16 birds, *Salm. Thompson* from 10, *Salm. anatum* from 2, and *Salm. enteritidis* and *Salm. Cubana* each from one; *Salm. Thompson*, *Salm. typhi-murium* and *Salm. Worthington* were each isolated from edible offal on one occasion; *Salm. Worthington* and *Salm. anatum* were each isolated once from the gloved hands of operatives engaged in evisceration. *Salm. Kentucky* and *Salm. Poona* also were isolated from chill tanks. 41 water samples from scald and “other” tanks were negative. On occasions when salmonellae were isolated they were found in a number of specimens collected simultaneously, but from 10 of 23 visits 251 samples were negative. Opportunity for dissemination occurred during evisceration and chilling.

It is suggested that the most effective way to exclude salmonellae from broiler-processing plants will be to eliminate them from the feeding-stuffs of young chickens.

Betty C. Hobbs

ANGELOTTI, R., FOTER, M. J. & LEWIS, K. H. **Time-Temperature Effects on Salmonellae and Staphylococci in Foods. I. Behavior in Refrigerated Foods.** *Amer. J. Pub. Health.* 1961, Jan., v. 51, No. 1, 76–83, 3 figs. **II. Behavior at Warm Holding Temperatures.** *Ibid.*, 83–8, figs. 4–6. [34 refs.]

I. Mixed cultures of *Salm. Senftenberg* 775W, *Salm. enteritidis*, *Salm. Manhattan* and mixed cultures of *Staph. aureus* strains 196E and MF 159 and MS 149

were inoculated into custard, chicken à la king, and ham salad—10 million organisms per gm. into 50 gm. of food. The inoculated samples were incubated for 5 days at temperatures varying by 2°F, from 40°–50°F, and at 95°F. Plate counts were made on 10 gm. quantities of food removed at 24-hour intervals; control samples were also examined.

There were significant differences between the growth of salmonellae and staphylococci in the different foods at different temperatures. In custard staphylococci grew at temperatures of 44°F. and above, but the salmonellae gradually decreased in numbers at all temperatures from 40°–50°F.

In chicken à la king, both salmonellae and staphylococci grew at temperatures of 44°F. and above.

In ham salad there was no growth of either organism from 40°–50°F. At 95°F. both groups of organisms grew.

It was concluded that the growth of staphylococci and salmonellae is inhibited in perishable food at temperatures at or below 42°F.

II. The same mixture of organisms and the same foods were used for testing the growth of the organisms at 95°F. and at 2°F. intervals from 112° to 120°F. Counts were done at 6-hour intervals.

In custard, both groups grew at 114°F. but decreased in numbers at 116°–120°F. In chicken à la king, the staphylococci grew at 112°F. but were killed at higher temperatures; the salmonellae grew at 114°F. but were killed at higher temperatures. In ham salad both groups decreased in numbers at temperatures of 112° to 120°F. There was a good growth at 95°F.

As the growth of both salmonellae and staphylococci in the foods tested occurred between 44° and 114°F., it was recommended that perishable foods should not be stored for any length of time permitting growth in the mid-portion of this range.

Betty C. Hobbs

PUBLIC HEALTH LAB. SERVICE. *Brucella abortus* in Milk in England and Wales in 1959. A Report. *Monthly Bull. Ministry of Health & Pub. Health Lab. Service* (directed by *Med. Res. Council*). 1961, Feb., v. 20, 33–6.

Reports on *Brucella abortus* in milk were submitted by 35 laboratories in England and Wales during the course of routine examination of mixed milk from individual herds for tubercle bacilli. The sediment from 50 ml. samples of milk was mixed with 1 ml. butterfat and injected intramuscularly into the thigh of a guineapig; after 6 weeks the animal was killed and examined for tubercle bacilli. At the same time the regional lymph nodes and the spleen were cultured for organisms of the *Brucella* group which were found in 544 (4·8%) of 11,450 samples of herd milk. Of 390 strains 93·6% were *Br. abortus* or one of its varieties, and 6·4% *Br. melitensis*.

A regional analysis showed that infection was highest in the North-West and lowest in the South-West.

A comparison is made with a figure of 11·29% reported in 1956 [this *Bulletin*, 1956, v. 31, 908]. It is suggested that because infected animals do not all excrete *Br. abortus* in milk, or may do so intermittently, the real incidence of herd infection in England and Wales is about 15%.

Betty C. Hobbs

ROBERTSON, L. *Brucella* Organisms in Milk. *Roy. Soc. Promotion Health J.* 1961, Jan.–Feb., v. 81, No. 1, 46–8. Discussion 48–50.

This is a communication given at a Sessional Meeting of the Royal Society of Health at Barrow-in-Furness in July 1960 and is concerned with the potential dangers arising out of the consumption of raw milk containing brucella organisms. The first part of the paper deals with the author's own experience of the bacteriological examination of milk from dairy herds in the northern part of Lancashire which were submitted to the Public Health Laboratory, Preston, during 1959. All the milk came from tuberculin-tested (TT) herds and milk from the majority of these herds was sold to the public, in whole or in part, as TT raw milk. The results show considerable variation, according to the particular area supplying the milk, in the percentage of specimens from which brucellae were isolated (9–30·9% with a mean figure of 18·7%). Typical *Brucella melitensis* were found in 1·9% of the herds examined. In most of the large towns nearly all the milk is heat-treated, but in the rural areas of northern Lancashire the greater amount of the milk is sold as TT raw milk and in some of the small isolated country townships almost none of the milk is heat-treated.

In considering the dangers arising from the consumption of raw milk the author was naturally more concerned with the protection of the rural population. Although it was obvious that the ultimate solution of the problem depended on the eradication of the disease in cattle, and as a preliminary step calf-hood vaccination was to be recommended, the immediate step should be further education of the public to demand universal pasteurization of milk supplies. There was a good discussion after the paper in which five of the participants spoke at some length.

[This paper did not present anything startlingly new but it makes interesting reading and the problem was well set out. At the present time although we are well aware of the high infectivity of the diseased animals themselves and the risks of close association with them, our knowledge of the actual infectivity of milk containing brucellae, as normally consumed by the general public, is very inexact. Nevertheless such milk must be regarded as potentially dangerous and few would disagree with the author's plea for universal heat treatment for the removal of this risk.]

H. J. Bensted

FOOD POISONING

DOLMAN, C. E. **Further Outbreaks of Botulism in Canada.** *Canadian Med. Ass. J.* 1961, Jan. 28, v. 84, No. 4, 191-200, 1 fig. [32 refs.]

In 1954-60 there were 10 outbreaks of botulism in Canada, 6 of the episodes occurred in Labrador, and 15 of 24 persons died; of the *Cl. botulinum* strains isolated, 4 were Type E and one each Types A and B.

In 1919-53 14 outbreaks were reported, Types A and E in 3 instances each; from the 24 outbreaks in 40 years 50 of 87 persons died (57.5%).

In 18 outbreaks the food vehicle was inadequately cooked or was pickled fish, raw fish eggs with unsanitary preparation, or products of sea mammals, especially seal and white whale.

In the U.S.A. in 1899-1949 there were 477 outbreaks, 830 of 1,251 (65%) persons died, and canned vegetables and Type A strains predominated [see this *Bulletin*, 1951, v. 26, 799]. Comparative figures for other countries including Russia, France, United Kingdom, Norway, Denmark and Japan are also given.

In Canada and Japan, Type E outbreaks predominate, occurring in areas where dietetic customs entail consumption of uncooked fish products after storage, provided Type E spores occur in the local environment, e.g., shore, sand, sea mud and nearby soil in Alaska, North-west territories and Labrador. Routes of contamination may be endogenous (intestinal) or exogenous (soil). Type E botulism is described as a rapidly progressive afebrile illness with abdominal disturbance, general weakness and malaise, with evidence of cranial palsies occurring within 8-20 hours after consuming uncooked products of fish or sea mammals. Death frequently occurs in less than 24 hours and rarely after 3 days. The rapidity of onset and death may be explained by the activation of Type E toxin by trypsin in the upper gastro-intestinal tract at pH 5.5-6.5. Type B toxin is less sensitive and Type A not at all sensitive to trypsin, so that the incubation period and time to death for these toxins are longer. Some of the clinical differences between botulism and other infective and toxæmic conditions are given. It is emphasized that wherever botulism is endemic the peculiar combination of persistent lassitude or weakness, constipation, fuzziness of vision or difficulty in accommodation and perhaps slight dysphagia, should arouse suspicion of botulism; the diagnosis should be verified by isolation from vomitus or stomach contents of a heat-labile toxin neutralizable by A, B or E anti-toxin or the organism. Food, however stale or fragmentary, should be examined, or samples from the same batch of canned, bottled or otherwise preserved food. Toxin may also be demonstrated in blood, and organisms from faeces, or from spleen or liver at post mortem.

Treatment is given in detail—the most important factors being evacuation or destruction of toxin in the stomach and intestines and neutralization of circulating and neurologically fixed toxin. It is stressed that type-specific or polyvalent antitoxin must be readily available; also a mechanical respirator.

The author gives a warning that home processed vegetables and fruit grown on soil containing Type A spores (which are heat-stable) are dangerous; Type E spores are relatively heat-labile, but raw or lightly cooked foods are a menace, and furthermore recontamination may also take place.

Type E strains multiply and produce toxin at 6°C. and the optimum temperature range for growth and toxin production is 5°-10°C. lower than for Type A and B strains, so that storage at relatively cool temperatures will be ineffective. Smoking, drying, pickling and salting cannot be regarded as safeguards. The soundest prophylactic measure is thorough exposure of food to 80°C. for 20 minutes or 90°C. for 10 minutes within 1-2 hours of consumption, otherwise the people should be educated away from dangerous diets. *Betty C. Hobbs*

FARAJ, A. & HUGONOT, R. Intoxication collective groupant 10,000 cas par une huile contenant des crésyl-phosphates. Problèmes d'organisation. [An Epidemic of 10,000 Cases of Poisoning by Oil containing Cresyl Phosphates] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1961, Jan.-Feb., v. 9, No. 1, 28-35, 3 figs.

This paper contains an account of the investigation of and official action taken in the epidemic of 10,000 cases of cresyl-phosphate poisoning in Morocco during September to December 1959 [this *Bulletin*, 1960, v. 35, 241] which is second in magnitude only to the well-known epidemic in the United States in 1930 [*ibid.*, 1931, v. 6, 99, 207, 443, 717; 1932, v. 7, 389, 585].

There are descriptions of the 3 stages in the official inquiry and subsequent action:—(1) the stage of research to discover the aetiology of the cases of polyneuritis, (2) the stage during which the distribution of the toxic oil, discovered to be the cause, in Morocco was investigated and scientific study of the whole epidemic was organized and (3) the stage of organizing the re-education of paralysed patients.

The clinical picture is described in brief. Cases of poisoning were concentrated in the regions of Meknès and Rabat (there is a map to illustrate this). At first the causation of the symptoms was obscure and chemical analyses of many different foodstuffs provided no light but ultimately the cause was found to be oils used for food which had been adulterated with 6 to 13% of surplus mineral oil containing cresyl phosphates. Vigorous action was taken to seize these dangerous oils and to prevent their appearance on the market.

There is also a description with a diagram of the organization of services for the treatment and re-education of the large number of patients with residual paralyses.

[See also this *Bulletin*, 1960, v. 35, 771.]

M. E. Delafield

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

LACAZ, Carlos da Silva. **Manual de micologia médica** [Manual of Medical Mycology]. 3rd Edition. 559 pp., 270 figs. 1960. Rio de Janeiro. São Paulo: Livraria Atheneu S/A.

The latest edition of this work is on similar lines to the earlier ones [this *Bulletin*, 1953, v. 28, 592; 1956, v. 31, 767] but it has been extensively revised and supplemented. There are 137 more pages and 108 more figures than in the previous edition, and the paper is of better quality. Among the additions is a chapter on mycoses of veterinary interest and another on the pathological anatomy of mycoses. The bibliography has been much enlarged and a glossary of mycological terms has been added.

This comprehensive manual, which covers more than Brazilian conditions, is now the standard Portuguese text in its field.

G. C. Ainsworth

CASTELLANI, A. **Long Term Observations on Pathogenic Fungi in Culture.** *J. Trop. Med. & Hyg.* 1961, Mar., v. 64, No. 3, 60-63.

The author discusses the well known tendency of pathogenic fungi maintained on artificial media to undergo pleomorphism and so lose most or all of their original specific characteristics. Using material subcultured about once a month on 4% dextrose agar till 1930, and thereafter on 2% dextrose agar, he divides fungi of human origin into 3 groups according to their stability on artificial media:—

1. Those whose characters change minimally or not at all over the years; e.g., various yeasts.

2. Those whose characters change but which eventually revert to the original state, e.g., *Geotrichum matalense* Castellani, 1915.

3. Those whose characters change permanently and irreversibly; e.g., most dermatophytes.

The author reminds us of a simple method for maintaining pathogenic fungi morphologically stable in distilled water for long periods (a year or more) and suggests that this technique is better than lysolytic [by which "lyophilic" is presumably meant] procedures. While maintenance of cultures in distilled water inhibits pleomorphic tendencies, it does not cause strains already pleomorphic to revert to the original state.

Ian G. Murray

D'ARCY, P. F., HOWARD, E. M., MUGGLETON, P. W. & TOWNSEND, Shirley B. **The Anti-Inflammatory Action of Griseofulvin in Experimental Animals.** *J. Pharmacy & Pharmacol.* London. 1960, Nov., v. 12, No. 11, 659-65, 2 figs. [15 refs.]

On the basis of some previous reports [this *Bulletin*, 1959, v. 34, 335, 656] that inflammation in ringworm lesions in man and animals rapidly subsided when oral griseofulvin was administered, a study of this alleged anti-inflammatory effect of griseofulvin was undertaken, rats, mice and guineapigs being used as experimental material. For comparison, the effects of administering cortisone or hydrocortisone acetate to these animals were also studied. Methods used were: cotton pellet test in rats; the tuberculin sensitivity test in guineapigs; the formalin foot test in rats; the cold stress test in mice; the test for protection of histamine-sensitized mice; the liver glycogen-deposition test in mice and lastly, the effects of griseofulvin on the adrenal cortex.

Results of griseofulvin administration associated with the foregoing tests were as follows: inhibition of the formation of granulation tissue around subcutaneously implanted cotton pellets; a reduction skin sensitivity to tuberculin; inconclusive effects resulting from the formalin foot test; no protective action against cold stress; no protection of mice sensitized to histamine; no glycogen deposition and no effect on the weight and histological appearance of the adrenal cortex.

C. J. La Touche

GOLDMAN, L., BEYER, Amanda & SCHWARZ, J. **Absence of Local Cytotoxic Change in Man from Griseofulvin.** [Correspondence.] *Nature.* 1960, July 23, v. 187, 335.

In view of the results obtained by PAGET and WALPOLE (*Nature*, 1958, v. 182, 1320) which showed that massive parenteral administration of griseofulvin interfered with mitosis, the authors decided to develop a technique for studying possible local cytotoxic reactions in man as a result of locally injected griseofulvin. The method consisted in injecting small quantities of a super-saturated solution of microcrystalline griseofulvin into areas of normal skin and into 3 cutaneous neoplasms of various types. The drug was also tested for its possible local inflammatory effect by injecting it in the form of a saline suspension into areas of psoriasis and neurodermatitis.

Results showed that the drug did not exhibit any demonstrable anti-inflammatory activity and did not itself give rise to any significant inflammatory reaction apart from a mild foreign body type of reaction around the injected crystalline substance, which usually subsided in 3 or 4 days.

No mitotic changes were observed as a result of local injections of the drug into normal skin, nor was any effect observed on the various tumours into which it was injected.

C. J. La Touche

BARICH, L. L., NAKAI, T., SCHWARZ, J. & BARICH, Donna J. **Tumour-promoting Effect of Excessively Large Doses of Oral Griseofulvin on Tumours induced in Mice with Methylcholanthrene.** [Correspondence.] *Nature*. 1960, July 23, v. 187, 335-6.

In pursuance of previous work which showed that griseofulvin in large doses had an arresting effect on mitosis in certain organs of the rat, the authors decided to test the effect of this drug on tumour formation in the epidermis of mice induced by surface applications of methylcholanthrene. The mice were divided into 5 groups. In groups 1, 2 and 3 one drop of 0.5% 3-methylcholanthrene in acetone was applied twice a week for 4 weeks to the lower back.

In group 1 the mice received a standard diet as well as applications of methylcholanthrene. In group 2 the mice received a 1% griseofulvin mouse food mixture for 6 weeks before, during and after applications of methylcholanthrene. In group 3 the mice received a 0.5% griseofulvin mouse food mixture for 6 weeks before, during and after applications of methylcholanthrene. In group 4 the mice received a 1% griseofulvin mouse food mixture for as long as group 2, but no methylcholanthrene; while in group 5 the mice received a 0.5% griseofulvin mouse food mixture for as long as group 3, without methylcholanthrene.

The results of these experiments showed that no tumours developed in groups 1, 4 and 5, whereas in group 2 papillomas developed in 6 of the 10 mice, and in group 3 tumours developed in 2 of the 10 mice.

When, in an additional experiment, mice were given griseofulvin in very small doses (0.01% or 0.1% griseofulvin food mixture) associated with the application of methylcholanthrene, no tumours developed. The authors emphasize the fact that the dosage in the 1% experiments was about 100 times as high as the dosage used in man.

C. J. La Touche

SCOTT, A. **Behaviour of Radioactive Griseofulvin in Skin.** [Correspondence.] *Nature*. 1960, Aug. 20, v. 187, 705-7, 1 fig.

In order to demonstrate photographically areas of concentration of griseofulvin in epidermal structures of subjects treated with this drug, the author undertook some investigations, using rats as test material, in addition to human subjects.

In a first set of experiments the author administered radioactive griseofulvin by mouth to rats (griseofulvin-chlorine-36 of specific activity 6.7 μ c. per gm.). The skin of some of these animals was finally subjected to radioassay and spectrophotometric analysis, while that of others was sectioned and stained with eosin prior to autoradiography by exposure of the section to Kodak AR. 10 and AR 50 autoradiographic film.

The control rats for this first series were not treated with griseofulvin but received DL-cystine-sulphur-35 with specific activity 31 μ c. per m.mole.

In a second series of experiments griseofulvin was administered in a 10% radioactive preparation topically to the skin surface of 2 normal human subjects and to

the tinea lesions of 8 infected patients. At 8 hours later the amount of the radioactive substance was assayed with a Geiger counter and biopsies were examined by autoradiography.

Results showed that, in the first series with normal rats, the griseofulvin was limited almost entirely to the hair follicles, "only those in the anagen phase of the growth-cycle contained radioactive grains, and of these, only 1 in 10". In the suprabulbar region 3 separate bands of deposition of radioactive material were seen.

In the second series autoradiographs showed a denser deposition of radioactive material in infected stratum corneum as well as in infected hair follicles. In normal skin the pattern of deposition of the radioactive material was relatively scant whereas in lesions it was present in nearly all the hair follicles infected with the dermatophyte and it was present in relatively higher concentration in infected areas of the stratum corneum.

The distribution of DL-cystine-sulphur-35 in the controls corresponded closely with that observed in the rats treated with griseofulvin, and hence it was concluded that griseofulvin was taken up during the formation of keratin although not intimately involved in its manufacture. It was also concluded that, during the process of translocation, griseofulvin remained relatively intact, and lastly, that its concentration in infected sites might be due to its affinity for the "associated partial degeneration of infected keratin" in the interstices of which it could accumulate and thus exert its fungistatic action.

C. J. La Touche

ARCH. DERMAT. 1960, May, v. 81, No. 5, 649-882, numerous figs. [Numerous refs.] **Griseofulvin and Dermatomycoses: an International Symposium sponsored by University of Miami, October 26-27, 1959.**

At a symposium on griseofulvin held at the University of Miami in October, 1959, numerous aspects of the biological and therapeutic effects of this drug were dealt with in papers and discussions.

The symposium began realistically with a note of warning in the opening paper which announced the existence of *in vitro* resistance to the drug in some strains of dermatophytes.

In metabolic studies in mice it was shown that maximum concentration of the drug in serum and blood was reached in 6 to 8 hours.

Bioassay of the drug at different depths of the human stratum corneum, using as test material germinating macroconidia of *Microsporum gypseum*, revealed the fact that the maximum retarding effect on germination produced by orally administered griseofulvin occurred when the macroconidia were applied at the junction of the stratum corneum and the stratum mucosum.

Electron microscopy revealed clearly the destructive action of the drug on the hyphal cell wall and its ultimate effects on the hyphal cytoplasm. Results of cytological investigations also suggested interference by the drug in the synthesis of nucleic acid in the fungal hyphae.

The effects of griseofulvin on the host were demonstrated experimentally by feeding different doses of it

to mice: large doses inhibited normal growth and development in these animals, whereas small doses resulted in their increase in weight during the first 10 days. Large doses, moreover, adversely affected spermatogenesis, but as such doses corresponded to 60-fold the therapeutic dose usually administered to human subjects this result was of merely academic interest.

In guineapigs it was found that, after a period of treatment lasting 23 days, quantities of the drug weighing up to 5–6 μ gm. could be extracted from the hair, and it was concluded from this that orally administered griseofulvin was deposited in the keratin of the hair shaft in an active and unchanged state.

Infection in guineapigs due to *Microsporum canis*, as estimated by biopsies, was cleared in 7 days, and in dogs in 13 days, while infection in dogs due to *Trichophyton mentagrophytes* was cleared in 20 days. Cures were also claimed for cats within periods varying from 2 to 8 weeks.

Observations based on serial sections of biopsies taken from the scalps of children suffering from tinea capitis due to *M. audouini* and treated orally with this drug showed that griseofulvin influenced the level on the hair shaft at which spores were formed, and that spore-bearing mycelium was eliminated from the hair at stratum corneum level at 35 days after the initiation of treatment.

Cures in cases of tinea capitis due to *M. audouini* were effected in 36 days when amounts of 0.25 gm. per day were administered orally, and tinea capitis due to *Trichophyton tonsurans* or *T. violaceum* was cleared within 3 to 5 weeks in almost 100% of cases.

The treatment of tinea pedis was unsatisfactory, but a combination of oral griseofulvin with traditional topical treatment was more successful.

The rate of cure in onychomycosis due to dermatophytes, especially *T. rubrum*, was shown to be dependent on the rate of growth of the nails, and, in so far as this was much faster in finger nails than in toe nails the response to treatment was correspondingly much quicker in finger nails than in toe nails, cures being effected in finger nails within 12 to 20 weeks, whereas a much longer period was necessary to achieve this result in the case of toe nails.

Widespread granulomatous lesions in a patient which were due to *T. rubrum* responded most satisfactorily to oral griseofulvin treatment.

All cases of favus due to *T. schoenleini* treated with oral griseofulvin responded very favourably.

Other mycotic skin infections such as pityriasis versicolor and erythrasma did not respond to treatment with oral griseofulvin.

When griseofulvin treatment of some deep mycoses was attempted results varied considerably. In the case of sporotrichosis there was a favourable response, but it was felt that it was not sufficiently marked or consistent to warrant the abandonment of potassium iodide therapy which is specific for this disease. Good results were also claimed for some cases of mycetoma due to *Nocardia brasiliensis*.

Undesirable but minor side effects of oral griseofulvin treatment which were mostly of a transient nature and which rarely necessitated abandoning treatment with this

drug, were noted by many observers, but were not sufficiently significant to cause anxiety.

In conclusion, it was generally conceded that oral griseofulvin treatment of dermatophyte infections is a major advance in the control of these diseases and that their eradication could be foreseen, at least in some parts of the world, through the use of this valuable drug.

C. J. La Touche

MORTON, Mary. **Superficial Mycoses in Melbourne.**

Med. J. Australia. 1960, June 25, v. 1, No. 26, 1006–14. [16 refs.]

The author undertook this 18-months survey of superficial mycoses in Melbourne in order to establish what percentage of skin infections in that area were due to fungi and also to ascertain the different species concerned, as well as their relative proportions.

Results obtained included a number of dermatophyte species commonly found in sites of election on the body and frequently reported in surveys in other countries, viz., *Microsporum canis*, *M. audouini* (dysgonic type), *Trichophyton rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*, *T. sulphureum*, *T. schoenleini* and *E. floccosum*; and in addition to these fungi, *Candida albicans*.

Microscopic examination of material was made after it had been mounted in caustic potash solution (30% solution in the case of skin scrapings, 30% solution in the case of nail scrapings, and 7% in the case of hair stumps). In the case of nail shavings, the solution of caustic potash containing them was incubated for 1–2 hours at 37°C. before microscopic examination.

Results obtained with this microscopic technique were positive in only 197 out of 612 specimens obtained or submitted for examination.

Cultures were made by planting skin, hair or nail debris in 4 inocula on each of only 2 malt agar slopes, one containing antibiotic and the other without antibiotic. These slopes were then incubated at between 26° and 30°C.

By this technique positive culture was obtained from only 235 specimens out of a total of 612 specimens in the main survey.

The number of positive microscopic findings relative to the number of positive cultures is unusually low and may be due to the use of too high concentrations of caustic potash in the solutions used in the preparation of the skin and nail material.

Of special interest in this survey was the relatively high incidence of *M. canis*, not only in tinea corporis lesions but also in tinea pedis lesions (toe clefts and soles). Also of interest was the absence of *T. rubrum* in a total of 5 cases of tinea cruris where *Epidermophyton floccosum* was found in 4 and *Candida albicans* in 1 of the lesions, despite a relatively high incidence of tinea pedis due to *T. rubrum*.

The results are discussed very fully and set out in 6 tables.

C. J. La Touche

See also p. 628, SIMON [Distribution and Control of Foot Mycoses with special reference to Bituminous Coal-Mine Conditions].

MARSHALL, J. & BREDE, H. D. **Black Piedra in a Child with Pili Torti, Bamboo Hair and Congenital Ichthyosiform Erythroderma.** *South African Med. J.* 1961, Mar. 18, v. 35, No. 11, 221-5, 10 figs. [17 refs.]

The author describes from South Africa a case of black piedra in a white girl 4 years old which was shown by culture of the organism to be due to *Piedraia hortai*. The girl developed generalized cutaneous moniliasis soon after birth and a condition of congenital ichthyosiform erythroderma persisted thereafter. The patient's piedra was first diagnosed at the age of 4 years when two congenital abnormalities of the hair were also noted—bamboo hair (NETHERTON, *Arch. Dermat.*, 1958, v. 78, 483) and trichotortosis. A month of griseofulvin 0.5 gm. daily produced no improvement.

Black piedra is extremely common in the pelts of primates of Africa but this is the first unequivocal report of its occurrence in man on that continent.

Ian G. Murray

NEGRONI, P. **Micosis profundas (cutáneas y viscerales).** Vol. II. **Histoplasmosis.** *Histoplasmosis en La Argentina.* [Deep Mycosis. Vol. II. **Histoplasmosis, with an Account of Cases in Argentina**] 143 pp., 34 figs. [Numerous refs.] 1960. La Plata: Comisión de Investigación Científica, Provincia de Buenos Aires.

This work is generously planned. Vol. 1 (*Los Micetomas*, 1954. Buenos Aires; El Ateneo) was devoted to actinomycosis and to mycetomas caused by actinomycetes and by fungi, in Vol. 2 histoplasmosis (*Histoplasma capsulatum*) is reviewed. After a series of chapters summarizing the general characteristics, symptomatology, pathology, animal infections, allergy and immunity, mycology, and diagnosis of histoplasmosis, 51 cases from Argentina are tabulated and discussed. This useful volume, for those who read Spanish, ends with a 12½-page bibliography and a general index. G. C. Ainsworth

JACKSON, D. **Histoplasmosis. A "Spelunker's" Risk.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 261-3, 1 fig.

This is the story of 2 men who visited a bat-infested cave in the state of Coahuila, Mexico. Two weeks later one developed a short unidentified illness and the other developed histoplasmosis (diagnosed by clinical features, X-ray, skin and complement-fixation tests). He was given a little Amphotericin B which had to be abandoned owing to side reactions; nevertheless he recovered completely.

No attempt was made to culture *Histoplasma capsulatum* from either the patient or bat droppings and cultural study of limestone from the cave was negative. This is another illustration of the risk inherent in visiting bat-infested caves in areas where histoplasmosis is endemic, it being no strain on the imagination to attribute this man's illness to his speliological activities.

Ian G. Murray

AKRAWI, Y. Y. **The Biology of Intestinal Moniliasis.** *J. Facul. Med. Baghdad.* 1960, Apr., v. 2 (n.s.), No. 2, 63-9. [24 refs.]

This is a survey of the yeast flora of the intestine in normal subjects and in patients suffering from various diseases.

Results showed a high incidence (86%) of *Candida* spp. in stools of 200 normal patients, viz. *C. albicans* in 140 patients' stools; *C. tropicalis* in 28; *C. krusei* in 2 and *C. stellatoidea* in 2. The number of colonies in positive cultures varied between 1 and 5 and all colonies from the same stool belonged to the same species. There was also no significant age distribution and the earliest age at which positive cultures were obtained was between 7 and 10 days.

Results from an investigation of 473 selected patients in whom abundantly positive stools were found showed that in 113, other pathogens were also present, and that in 60 no reliable medical history could be obtained. These two categories of patients were therefore discarded, leaving 300 for further investigation.

In the remaining 300 the following clinical data were considered to be significant relative to the incidence of *Candida* in the stools: (a) "history of taking antibiotics within 10 days of the beginning of the enteritis", 265; (b) "uncontrolled diabetes mellitus with acetone-bodies in the urine", 8; (c) "various malignant conditions with marked cachexia and diarrhoea", 14; (d) "treatment with cortisone or ACTH", 13.

The significance of some of these clinical data was shown in the following way: (a) withdrawal of antibiotics was followed by the disappearance of symptoms of enteritis and the return to a number of bacterial and yeast organisms; (b) withdrawal of corticoids was likewise followed by a cessation of symptoms of enteritis.

The species distribution in these groups of patients was: *C. albicans* in 239 patients; *C. tropicalis* in 53; *C. krusei* in 5; *C. stellatoidea* in 3. Again in this series only one species was found in the stools of any given patient.

It was also noted that the reaction of the stools was highly acid in 95% and that this was also the case in normal infants below the age of 6 months.

C. J. La Touche

WILLI, H. **Generalisierte Moniliase der Haut bei einem Neugeborenen.** [Generalized Moniliasis of the Skin in a New-born Child] *Schweiz. med. Woch.* 1961, Mar. 25, v. 91, No. 12, 376-9, 4 figs. [10 refs.]

Monilia infection of the skin in the new-born has been described in a number of papers [this *Bulletin*, 1956, v. 31, 716; 1958, v. 33, 846] but the account of such a case is here presented as it has characters of interest. There is a full clinical description with a number of photographs.

On the 5th day of life numerous small blisters, with yellow contents, appeared on the infant's head. The blisters spread to many parts of the body and in some sites developed a vesiculo-papular character. No lesions were seen in mouth or throat. The condition improved rapidly after treatment by potassium permanganate baths and the child was discharged from hospital when

3 weeks old. There is a full account of the investigations which confirmed the diagnosis of *Candida albicans* infection.

The source of the infection is not absolutely clear but is presumed to have been the mother from whose vagina the organism was isolated.

M. E. Delafield

GOLDMAN, H. J., LITTMAN, M. L., OPPENHEIMER, G. D. & GLICKMAN, S. I. **Monilial Cystitis—Effective Treatment with Instillations of Amphotericin B.** *J. Amer. Med. Ass.* 1960, Sept. 24, v. 174, No. 4, 359–62. [18 refs.]

Case reports of 2 male patients suffering from cystitis due to *Candida albicans* treated with amphotericin B instillations are given in this article.

The patient concerned in case 1 received instillations of amphotericin B by the following procedure: 15 mgm. of the drug were dissolved in 100 ml. of sterile water and the solution was injected into the bladder *via* a urethral catheter after the bladder had been evacuated. The patient was then instructed to refrain from micturating for as long as possible. This treatment was administered daily for 11 consecutive days. The patient also received an alkalinizing mixture every 4 hours. After 3 days of such treatment symptoms of urgency, frequency and dysuria showed a marked decrease. At the end of this course of treatment all symptoms had disappeared. Moreover, all cultures of urine specimens taken after the fifth instillation were negative for *Candida*, but bacteria were present; these had disappeared 5 months later.

The patient in case 2 was given daily instillations, for 8 days, of 15 mgm. of amphotericin B dissolved in 400 ml. of sterile water. He showed symptomatic improvement after 3 or 4 such instillations and urine cultures became sterile.

C. J. La Touche

SILVA, M. E. **Occurrence of *Cryptococcus neoformans* and *Microsporium gypseum* in Soils of Bahia, Brazil.** *Bol. Fundação Gonçalo Moniz. Bahia.* 1960, July, No. 17, 7–14, 2 figs. on pl. [23 refs.]

The purpose of this paper is to report the isolation of *Cryptococcus neoformans* and *Microsporium gypseum* from soil in the state of Bahia, Brazil.

90 specimens of soil from the city of Jacobina, deliberately taken from inside and around chicken runs and pig styes, were collected and examined by inoculation of extracts into mice and by hair baiting. Of these 90 specimens, 6 (6·7%) yielded *Cryptococcus neoformans* and 26 (28·9%) yielded *Microsporium gypseum*. The *C.*

neoformans isolated was found to be highly virulent for mice. This is the first report of *C. neoformans* and *M. gypseum* in the soil of Brazil, though diseases caused by these organisms have long been known to occur in that country.

Ian G. Murray

JEDLICKOVÁ-BESTÁKOVÁ, Zdenka, KOUBA, K. & ZÁMEČNÍK, S. K. **otázce patogenity *Nocardia asteroides*. [On the Pathogenicity of *Nocardia Asteroides*]** *Časopis Lékařů Českých.* Prague. 1961, Mar. 10, v. 100, No. 10, 300–305, 5 figs. [30 refs.]

The English summary appended to the paper is as follows:—

"The authors give an account of two patients with *Nocardia*, most probably *Nocardia asteroides*. The first patient had tonsillitis associated with an exanthema and eosinophilia; the second patient suffered from relapsing chronic adnexitis with fluor. In the present paper the author presents a detailed microbiological identification of the agent and discusses the possible participation of *Nocardia asteroides* in the clinical picture of the two patients."

LAKSHMIPATHI, G. & MURTI, B. R. **Otomycosis.** *J. Indian Med. Ass.* 1960, June 1, v. 34, No. 11, 439–41.

This is a short report of findings in 28 patients suffering from otomycosis.

The order of frequency of the symptoms associated with this condition was: pain in 27 patients, discharge in 13, defective hearing in 10, itching in 4 and tinnitus in 3. In 27 ears the tympanic membranes were intact, whereas in 3 "a central type of perforation was present".

Laboratory investigations included direct microscopic examination of material from the affected ear in 10% potassium hydroxide solution and culture of the material on various culture media including Sabouraud's agar.

The fungi isolated included *Aspergillus niger* in 18 ears, *A. fumigatus* in 11 ears and *Candida albicans* in 1 ear.

Treatment consisted in syringing the affected ear with warm sterile water after the material in it had been loosened with hydrogen peroxide, then drying it. After this, drops of spirit containing boric acid ("10 grains of boric acid in 1 oz. of rectified spirit") were instilled into it once daily for 1 week.

In most patients this treatment resulted in improvement within the first week.

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

MACGREGOR, I. M. **The Two-Year Mass Radiography Campaign in Scotland 1957–1958. A Study of Tuberculosis Case-Finding by Community Action.** pp. vii + 98, 16 figs. [49 refs.] 1961. Edinburgh: H.M. Stationery Office. [7s.]

During 1957 and 1958 mass radiography surveys were made in 21 areas of Scotland. The cities of Glasgow [population 1,081,665] and Edinburgh [population 466,889] were included, and the reports concerning them have already been noticed in this *Bulletin* [1959, v. 34, 426, 427].

The total population of Scotland was 5,123,336 in 1954 and 3,225,212 persons (63%) resided in the survey areas. 77% of the notified cases of tuberculosis and 77% of the deaths were in these areas.

It was estimated that some 1,200,000 adults would attend for X-ray examination, and that 600 mass radiography unit weeks would be required for the survey with the exposure on average of rather more than 2,000 miniature films per week. There were 7 self-contained mobile and 3 transportable Scottish units, and with the help of other United Kingdom health services 64 units were made available.

During the 60 weeks of the campaign 1,844,268 persons were examined. This was 50% higher than the expected response. After the deduction of non-residents and children there remained 1,639,957 persons aged 15 and over representing 68% of the defined population. The response rate in the 15 urban areas was 75% and in the 4 Scottish cities 76%. The number of adults examined represented 43% of the adult population of Scotland.

All persons with a significant pulmonary abnormality shown on the skiagram were referred to local chest physicians for further examination. The diagnosis and classification on which the results of the survey were based were made after a minimum follow-up period of 3 months.

12,094 new cases of pulmonary tuberculosis were discovered. The disease was regarded as active in 4,328 persons (2.35 per 1,000 examined) and 7,766 (4.29 per 1,000) presented evidence of tuberculosis which required observation. Nearly two-thirds of the new cases were found among residents of Glasgow and four-fifths in the 4 Scottish cities. The rates for active disease ranged from 0.26 to 3.69 per 1,000 and for disease requiring observation from 0.14 to 10.37. Active disease was found in 3.76 per 1,000 in Glasgow, in 1.71 in the other 3 cities, in 1.49 in towns and in 1.41 in rural areas.

When the discovery rates were considered in relation to the existing indices of the prevalence of tuberculosis

in the survey areas the degree of association was found to be low. The explanation of this unexpected finding presented is that physicians found difficulty in allocating patients to the active and observation groups. Limitations of staff and equipment prevented the use of dual reading of skiagrams which would have increased the discovery rate by some 10%.

Of the 4,033 new cases of tuberculosis identified among residents in the survey areas 1,131 (28%) were confirmed bacteriologically during the period of observation permitted. This was a yield of 0.67 per 1,000 persons examined (range 0.99 to 0.11). In the 4 cities the bacteriological results were less often positive in the survey cases than in those notified ordinarily and in Edinburgh the radiological appearances of the lesions were significantly less severe in the survey cases. This was an indication of the success of the campaign in finding disease at an early stage.

An attempt was made to estimate the prevalence of tuberculosis among persons who failed to co-operate. A supplementary survey was made in Edinburgh during which 526 persons (25% of the 2,156 non-attenders) were examined. The total yield of significant tuberculosis was significantly higher than in the main survey at all ages but the difference in the yield of active disease was statistically significant only between 35 and 64 years of age. Among females only those aged 65 years and over showed a higher prevalence in the supplementary than in the main group.

Analysis by age and sex showed that the total discovery rate of active disease in the whole survey was 3.22 per 1,000 in males and 1.83 in females; rates in the observation group were 5.48 and 3.31 respectively. Active disease in men was found with increasing frequency with advancing age (2.11 at 15–24 years and 4.9 at age 60 and over). The rates in women were 2.34 at 15–24 and 0.79 over 60. Observation rates in men were 1.74 and 10.28 respectively and in women 1.83 and 3.14 respectively. The most profitable sources of new cases were older men and younger women.

Tuberculosis was the condition most frequently diagnosed, being responsible for 25,375 of the abnormalities identified; bronchiectasis, emphysema and allied conditions were found in 4,956 patients, cardiac abnormalities in 4,338, pneumoconiosis in 2,529, and malignant tumours of the lung in 746 (0.43 per 1,000 in 1957 and 0.37 in 1958).

“The results of this campaign are regarded as an outstanding success in terms of public response and tuberculosis identification.” [Who will disagree?]

H. G. Calwell

BRUCE, T., DAHLBOM, L., DAHLSTRÖM, G., HEMRING, H., PEGELOW, K. & UGGLA, L. G. **Sociomedical Studies of Tuberculous Patients from Stockholm.** *Acta Tuberculosea Scandinavica*. 1960, Suppl. 50, 56 pp., 12 figs. [24 refs.]

Now that it is possible to treat successfully nearly all patients suffering from pulmonary tuberculosis provided that the disease is of reasonably recent origin it is necessary to consider what are the reasons for the failures and how they can be obviated.

Among the more important are social conditions and personality problems.

2 studies on these questions have been made at the City of Stockholm Chest Hospital at Söderby; the work amplified the well known paper by DALÉN and DAHLBOM (*Socialmed. tidskr.*, 1956, v. 33, 181): (1) The 250 persons who were in-patients at the hospital on November 10, 1958; (2) the 339 consecutive cases of active pulmonary tuberculosis admitted to hospital from March 1 to October 23, 1959, at the time of hospitalization.

The male patients were predominantly in the age-groups 45-65, while the female patients were usually 5-10 years younger. From the clinical point of view, diabetes was present in an abnormal proportion of patients, also patients who had had a resection for peptic ulcer were estimated in this study as 4 times the average. This excess has been the subject of disagreement between various authors.

In both series alcoholism was an important finding; 69 out of the 170 male patients in the first group and 45% in the second had a history of alcoholism, and about 16% and 27% in the 2 groups were chronic alcoholics. In females this was not a frequent problem. A high proportion of the male patients were unmarried or divorced, and in these the proportion of chronic alcoholics were abnormally high. The incidence of divorce among the female patients differed only slightly from that existing in the general population. Unsatisfactory housing conditions were common; for instance, 25% of the male patients in the first group were living in lodgings. Financially, 26% of the male patients were receiving public assistance at the time of admission to hospital, and a similar percentage occurred in the other group. In the first group it was considered that 25% of the males were out of employment or unsuitably employed. The proportion of mentally maladjusted patients was high. This was more apparent among the female patients (23% of 80 patients against 9% among the men). The reason for the difference was not clear but it was suspected that there was a tendency for the males to resort to alcohol in mental disturbance and that if the alcoholism had not existed more men would have been diagnosed as mentally unstable.

Sociotherapeutic measures are obviously necessary in view of these findings.

From the start of treatment, patients must have recreational and vocational training as there is great danger that even if the medical treatment is successful many of the patients are likely to be psychologically worse at the end of treatment than before.

In addition an attempt must be made to alleviate the social difficulties.

The provision of suitable work is of fundamental importance and it was found that reabsorption of the patients into the work they had done previously was most successful. Where this was impossible, training of men for new occupations was only suitable for those under 45 and in view of the greater numbers of men over the age a hard core of patients unlikely to be employed will remain.

It is surprising to read that the start of a sociotherapeutic department was not embarked on until 1946 when an almoner was appointed followed by a part-time occupational therapist in 1947, which appointment was made full-time in 1949. The staff was gradually augmented and in 1957 a consultant in occupational rehabilitation was appointed. The staff now consists of this official, an almoner, 1 educational and 2 occupational therapists, and 2 clerks. This department now has regular consultations with the ward physicians with the result that the clinicians are far more aware of the social and psychological problems. The relationship between the hospital staff and the chest clinics is unfortunately not referred to.

F. H. Young

SMITH, D. T., JOHNSTON, W. W., CAIN, Iva M. & SCHUMACHER, Muriel. **Changes in the Tuberculin Pattern in Students between 1930 and 1960.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 213-34, 7 figs. [64 refs.]

Between 1930 and 1940 about 60% of the second-year medical students in a university in North Carolina were found to react to 0.1 mgm. of OT, and an additional 20% to 1 mgm. Approximately 10% of the reactions to 0.1 mgm. measured 20-40 mm. and were vesiculated. After the beginning of the clinical training (with consequent exposure to tuberculous patients) the reactor rate increased to about 98% by the end of the fourth year of medical study.

Between 1940 and 1950 there was a gradual fall in the reactor rate which was accompanied by a decline in hypersensitivity and an increase in the proportion of those who reacted only to 1 mgm. of OT.

Since 1950 reactions of hypersensitivity have disappeared; the proportion of those reacting only to 1 mgm. has increased and the proportion of those reacting to 0.1 mgm. has decreased. In 1958-59 only 7.5% were found to be reactors to 5 TU of PPD-S while 39.1% reacted to 250 TU of PPD-S.

During the period of these observations there was a parallel change in the incidence of tuberculosis. The conditions in which massive infection and reinfection with tubercle bacilli were almost inevitable have ceased to exist in most parts of the United States. It could therefore be readily assumed that the changed pattern in tuberculin sensitivity is entirely due to the infrequency of the exogenous reinfections which formerly maintained a high level of sensitivity in the majority of the population.

The possibility that other bacillary factors play a part was studied by means of comparative tuberculin testing of white and Negro medical students and nursing students with OT, PPD-S, PPD avian, PPD-Y (photochrome bacillus) [this *Bulletin*, 1959, v. 34, 816] and PPD Battey.

The sizes of the reactions to the various antigens were compared and related to the geographical location of the subject. Support was found for the theory that a weak reaction to human tuberculin is virtually never due to infection with human tubercle bacilli and that such reactions are commoner in persons from the south-eastern than other parts of the United States. "Various biologic and epidemiologic facts discussed in this paper suggest that avian tubercle bacilli may play an important role in this heterologous sensitivity to tuberculin."

H. G. Calwell

SALOMON, H. & ANGEL, J. H. Corticotropin-Induced Changes in the Tuberculin Skin Test. A Controlled Study in Advanced Tuberculosis. *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 235-42, 2 figs. [45 refs.]

Patients with advanced or moderately advanced pulmonary tuberculosis were allocated at random to a group treated with corticotrophin in addition to specific anti-tuberculosis drugs or a control group receiving only specific chemotherapy. A total of 33 patients received corticotrophin while 30 acted as controls.

Both groups received 0.3 gm. of isoniazid, 12.0 gm. of PAS and 1.0 gm. of streptomycin daily for 6 months; in addition the corticotrophin group received corticotrophin gel intramuscularly, beginning with 80 units daily and decreasing to an average maintenance dose of 30-40 units daily for a total of 3 months.

The patients' tuberculin sensitivity was studied by Mantoux tests with 5 TU of PPD-S before treatment and at the 6th week and 3rd and 6th months of treatment. The greatest diameter of induration at 48 hours was recorded. The criterion of a positive reaction was induration of 5 mm. or more.

Before treatment both groups displayed comparable sensitivity. In each group there were 2 patients without induration and 5 in the control and 6 in the corticotrophin group with negative reactions. This indicated the advanced state of the disease and the poor general condition of many of the patients.

6 weeks after the start of treatment the mean induration of the reactions in the corticotrophin group was reduced to almost half that of the controls; at 6 weeks all patients in the control group reacted to tuberculin but 10 patients in the corticotrophin group were non-reactors, 8 of whom had no induration at all.

After 3 months' treatment, and after at least a week after the last dose of corticotrophin, there were no statistical differences between the groups, and at 6 months there were no demonstrable differences between them. All patients available for testing had reactions of more than 5 mm. of induration.

H. G. Calwell

McKEE, W. D. & FAVOUR, C. B. Immediate Component in Tuberculin Reactions. *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 243-7, 3 figs. [13 refs.]

The immediate type of reactivity to tuberculopoly-saccharide and to OT is thought to be mediated by the

carbohydrate component of OT reacting with a factor in gamma globulin. It can be transferred passively by the gamma globulin of tuberculin-sensitive guineapigs [this *Bulletin*, 1955, v. 30, 723].

In the experiments described this latent anaphylactic sensitivity (Arthus phenomenon) was demonstrated by administering tuberculin into a mildly hyperaemic site caused by a nonspecific reaction to killed yeast particles.

Guineapigs were sensitized by injections of heat-killed human tubercle bacilli, and hypersensitivity was maintained by repeated doses. 24 animals which had shown necrosis at the site of a Mantoux test with PPD were selected as experimental group A; 24 animals with tuberculin reactions of more than 5 mm. induration and no necrosis formed group B, and 16 normal animals served as controls.

4 days later when the tuberculin reactions had subsided nonspecific inflammation was produced by injections of yeast, one in each flank. At 18 hours a tuberculin test with 5 μ gm. in 0.1 ml. of PPD was superimposed at one yeast site and an equal volume of either saline or histoplasmin 1 in 100 was injected into the control yeast site. The diameters of erythema, induration and central blanching were recorded at 2, 4, 7 and 24 hours. Haemorrhage and oedema were noted when present and biopsy specimens of skin were taken for microscopic study.

The animals in group A showed an immediate type of reaction within 2 hours which was characterized by oedema, central blanching and haemorrhage. Those in group B showed early inflammatory reactions of smaller degree. A typical delayed reaction then followed. Control injections with histoplasmin and with saline had little effect on the yeast reactions.

Histological examination of the yeast sites showed moderate cellular infiltration. When saline was injected into these sites small increases in oedematous separation of the tissues were seen. The findings were similar when PPD was injected into the yeast sites in the control animals. In both groups of hypersensitive animals however increased cellular infiltration and oedema were seen during the first 7 hours. Both increases were much more prominent in group A animals. At 24 hours both test and control sites appeared similar in group A and group B animals. Reactions were characterized chiefly by an increase in mononuclear cells.

"It is postulated that the necrosis of severe tuberculin reactions is an immediate type of response superimposed upon a delayed type of hypersensitivity."

H. G. Calwell

See also p. 633, GROSS, WESTRICK & MCNERNEY, **Tuberculosilicosis: a Study of its Synergistic Mechanisms.**

KANN, G. Resultados del tratamiento ambulatorio de la tuberculosis en el Centro de Salud "La Paz". [Results of the Ambulatory Treatment of Tuberculosis at the La Paz Health Centre] *Rev. Salud Pública Boliviana.* 1960-61, Dec. 15-Jan. 15, v. 2, No. 2, 46-53, 2 graphs.

The author, who is the Director of the Tuberculosis Division of the Ministry of Health in Bolivia, first points

out that for the whole country with an estimated 50,000 cases there are only 1,000 beds for tuberculosis in hospitals and then gives the figures relating to a project to try to control the incidence of (pulmonary) tuberculosis in a part of La Paz (the capital) with an estimated population of 120,000, of high density. In addition the people were for the most part poor, a number were unemployed, most were not covered by the social security measures in force, malnutrition was evident, and general and individual hygiene almost non-existent. These conditions explain the high incidence of tuberculosis (over 10% in spontaneous consultations).

Unfortunately no records relating to previous years existed so that proper comparisons were not possible, but for the period 1 May, 1959, to 30 April, 1960, 494 proved cases [the figures in the amended text and in Table I do not agree] attended the clinic. The maximum incidence was in the 20-30 age-group with more cases in men than women, while the figures for the 30-40 group were still higher than for the 10-20 group. 260 were given ambulant treatment, 47 were admitted to hospital, 147 defaulted, and 7 died. Of the ambulant patients 60 had minimal, and 197 moderately advanced or advanced lesions. At the start 53% were sputum-positive, 34% negative, 13% not examined (mostly children). By the end of the treatment-year 57% of those originally sputum-positive had become negative.

Treatment consisted in the oral administration of 8 mgm./kgm. isoniazid daily with 1 gm. dihydrostreptomycin parenterally twice weekly. The results were: 15% had less than 3 months' treatment, 11% became inactive, 44% still active but improved, 2% probably active, and 2% probably inactive, 41% not improved (including the above 15%).

In addition 765 contacts of these ambulant cases were investigated and 638 kept under observation and dealt with as follows:—

- (a) healthy adults, 360—3-monthly X-rays.
 - (b) children tuberculin-negative, 80—BCG and 3-monthly X-rays.
 - (c) children tuberculin-positive, 168—prophylactic isoniazid and 3-monthly X-rays.
 - (d) with active pulmonary tuberculosis
 - (i) with minimal lesions, 4
 - (ii) advanced lesions, 15
 - (iii) very advanced lesions, 11
- } chemotherapy and X-rays

Of the 168 tuberculin-positive children none showed evidence of active disease and they were given 5 mgm./kgm. isoniazid daily [see below].

The author summarizes as follows: (1) 29.8% of the patients treated during the year defaulted; (2) 101 suffering from active tuberculosis refused treatment; (3) the high percentage of advanced lesions emphasizes the need for case-finding and treatment in earlier stages; (4) the chemoprophylaxis of the tuberculin-positive children was effective, since of 68 given 5 mgm./kgm. daily only 2 developed active disease, 2 died during treatment [nothing is said about the remaining 100]; (5) the results of this method are nearly as good as those obtained in hospital; (6) the cost was moderate. *W. K. Dunscombe*

JOHNSTON, R. N., SMITH, D. H., LOCKHART, W. & RITCHIE, R. T. **Optimal Dose of Streptomycin in Pulmonary Tuberculosis.** *Brit. Med. J.* 1961, Jan. 14, 105.

[Most authors have advocated streptomycin and isoniazid as the most efficient drug combination in tuberculosis, but the standard dose of 1 gm. daily of streptomycin as advocated in Great Britain leads to the development of vertigo and ataxia in an appreciable proportion of patients, especially the older age-group.] 135 patients were divided into 3 groups, comparable in severity and presence of cavitation. The first group (SI) received streptomycin 1 gm. daily, plus isoniazid 1,000 mgm. in 2 divided doses, with pyridoxine 50 mgm. twice daily. Group 2 (SP) received streptomycin 1 gm. daily, with pantothenic acid 150 mgm. daily at the same time, and isoniazid 100 mgm. twice daily. Group 3 (S $\frac{1}{2}$) received streptomycin 0.75 gm. [daily] plus isoniazid 100 mgm. twice daily. All patients received initially PAS 12 gm. daily for 6 weeks.

Positive pre-treatment cultures were obtained in 97 patients—32 in the SI group, 37 in the SP group, and 28 in the S $\frac{1}{2}$ group. The clinical improvement of all patients was satisfactory. The rate of sputum conversion after 1 and 3 months' treatment was similar in all 3 groups; by 6 months all patients were culture-negative and have remained so. A preliminary analysis of the radiological results on the first 88 patients who had completed 9 months' treatment shows similar degrees of improvement.

Vertigo developed in 14 of the 44 patients in SI group, in 12 out of the 46 in SP group, but in only 2 of the 45 in S $\frac{1}{2}$. Vertigo of a degree requiring cessation of streptomycin developed in 28 (21%) patients. The difference between the incidence of vertigo in the SI group (32%) compared with that in the S $\frac{1}{2}$ (4%) was statistically significant. Pantothenic acid is, in the authors' experience, of no value in preventing or diminishing the development of vestibular damage. They conclude that the reduction of the daily dose of streptomycin to 0.75 gm. nearly abolished the complication of vertigo, and was clinically adequate. *F. H. Young*

SIMPSON, J. MCD. **The Detection of Urinary Para-Aminosalicylic Acid with 'Phenistix' Reagent Strips.** *Tubercle.* 1961, Mar., v. 42, No. 1, 107-9.

SALIBA, A. & BEATTY, O. A. **Retreatment of Tuberculous Patients: an Experience with the Combined Use of High Doses of Isoniazid, Pyrazinamide and Cycloserine.** *Southern Med. J.* 1961, Jan., v. 54, No. 1, 10-16. [19 refs.]

This paper compares the results of 2 methods of therapy used on patients who had organisms resistant to 1 or more of the standard drugs. Group I consisted of 26 patients treated with pyrazinamide 500 mgm. 3 times a day, cycloserine 250 mgm. twice a day, and isoniazid 800 to 900 mgm. daily with pyridoxine 50 to 100 mgm. daily. Group II consisted of 15 patients treated with streptomycin 1 gm. daily for 3 to 6 months, isoniazid 800 to 900 mgm. daily with pyridoxine 50 to 100 mgm.

daily. PAS was added in some cases. The patients showed a predominance of far advanced disease; the predominant age in Group I was 40 to 59. Sputum examination was positive by smear and culture in all cases. In Group I no gross hepatic dysfunction was noted; the only serious complication was neuropsychiatric disturbance in 4 patients (15%), 3 of whom can be described as having an unstable personality. In Group II, 1 patient only complained of slight difficulty in hearing, by which time he was ready for the withdrawal of the streptomycin. Marked radiographic improvement was not noticed in Group I, whereas in 5 patients (33%) in Group II marked improvement was noted. The sputum in 30% of the first group was converted, as compared with 66% in the second group.

The authors advocate the use of streptomycin with high doses of isoniazid daily in treatment failures, and only to revert to pyrazinamide and cycloserine if this is unsuccessful.

F. H. Young

MOORE, M. J. & LEAVITT, D. **Fatal Hypersensitivity Reaction to Antituberculosis Medication.** *South-eastern Med. J.* 1961, Feb., v. 54, No. 2, 202-6, 3 figs. [12 refs.]

"A periarteritis nodosa-like illness, presenting as hepatitis, is described following combined streptomycin and isoniazid therapy. The literature with regard to reactions to the drugs used in the treatment of tuberculosis (PAS, isoniazid, and streptomycin) was briefly reviewed. Emphasis was placed on the frequent occurrence of hypersensitivity reactions with present-day medications and the need for suspicion of, recognition of, and treatment of these reactions when they occur."

LAWRENCE, S. H., WEIMER, H. E. & SALKIN, D. **Effects of Corticosteroid Administration of the Serum Electrophoretic Patterns of Patients with Pulmonary Tuberculosis.** *J. Lab. & Clin. Med.* 1961, Mar., v. 57, No. 3, 388-93, 1 fig. [16 refs.]

"During the study of the electrophoretic patterns of proteins and glycoproteins of patients recovering from pulmonary tuberculosis, it was noticed that those who received corticosteroids as an adjunct to therapy exhibited a markedly different protein response from those on antituberculosis drugs alone. Before treatment the serum proteins were lowered in the albumin fraction with increases in the α_2 and gamma components and elevated glycoprotein levels as is usually seen in extensive

exudative disease. Although comparable x-ray clearing occurred in the cortisone group, further increases in the α_2 , beta, and gamma globulin fractions occurred, while in the group not treated with cortisone these values returned to normal. The glycoprotein components of the group treated with cortisone declined during this period, indicating that the increases were due to carbohydrate-poor proteins. A statistical analysis is included."

NOHR, P. **Pulmonary Resection for Tuberculosis in Greenland. Preliminary Results of the First 478 Resections in the Course of Four Years.** *Danish Med. Bull.* 1960, Dec., v. 7, Nos. 7/8, 211-15. [14 refs.]

This paper reports the early post-operative results of 478 consecutive resections undertaken for tuberculosis from January 1, 1956, and the 4 ensuing years. The number of patients admitted to resection was 425, of whom 12.5% were submitted to bilateral resection. All patients received at least 4 months, and in most cases 6 months, pre-operative antibiotic treatment. 89 of the patients never had a positive sputum, 284 had a negative sputum for more than 3 months, and 52 a positive sputum for less than 3 months preoperatively. Radiological indications for resection were: regular infiltration—86; tuberculomata or filled cavities—164; cavities—218; destroyed lung—10. Of the resections, 14 were pneumonectomies; 45 lobectomies; and the remainder segmental resections or less.

Bacteriological investigation for *Mycobacterium tuberculosis* by culture was undertaken on 441 preparations. Only 43, or approximately 10%, of these were positive.

7 patients died during the first 4 weeks after operation; 3 of these deaths were due to haemorrhage, and 3 were due to accidents in connexion with the anaesthetic or the transfusion. All deaths occurred before an anaesthetist was appointed to the department.

The most important non-fatal complications in the 6 months of the post-operative period are given. Air leaks or space problems occurred in 14%; bronchopleural fistula in 2.9%; atelectasis in 10%; and haemothorax in 0.8%. Post-operative phychoses developed in 8 patients (1.7%).

Details of the methods of resection are given. The operative mortality in the material quoted is 1.5%, but in the year just concluded 150 pulmonary resections were undertaken without any operative mortality.

F. H. Young

VENEREAL DISEASES

McELLIGOTT, G. L. M. **Venereal Disease and the Public Health.** *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 207-15. [10 refs.]

The author, who was at one time adviser on Venereal Diseases at the Ministry of Health, traces the development of the venereal disease service since the report of

the Royal Commission set up in 1913; this latter advised against notification and this policy has been maintained ever since. Many will be surprised to learn that at that time the incidence of syphilis was estimated to be 10% of the population in the large cities; this figure is confirmed by a serological survey in 1914 when 10.3% of men and 5.1% of women in a small series were found to give positive blood reactions; in addition in 1908-12, 9% of all admissions to asylums had GPI and in 24.4% of children blindness was caused by gonorrhoea and in 31.2% by syphilis. The setting up and development of venereal disease clinics are discussed in some detail; both gonorrhoea and syphilis presented serious problems until the advent of the sulphonamides and later penicillin, though arsenicals and bismuth probably cured a great proportion of early cases of syphilis. Non-gonococcal urethritis (NGU) was becoming a problem even before the setting up of the National Health Service in 1948 and has speedily increased in gravity.

Though venereal diseases increased considerably towards and after the end of the last war they declined rapidly after 1946, but both gonorrhoea and NGU have increased in the last 4 years. Venereal disease appears to have become less and less important in recent times, but gonorrhoea, NGU and trichomoniasis alone justify the continued existence of treatment centres; the reservoirs of infection in women with latent gonorrhoea demand the services of many more social workers, NGU calls for more research and the increasing numbers of teenagers with venereal disease present a serious problem; more attention to the introduction of venereal disease into Britain by seamen seems called for. The venereal disease service still has an important part to play in the national economy.

T. E. Osmond

BRITISH CO-OPERATIVE CLINICAL GROUP [WILLCOX, R. R., Secretary.] **Age Groups of Patients with Infectious Venereal Disease, 1957 and 1958.** *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 216-26, 3 figs. With an Addendum on Findings related to Population Figures, 226-32, 2 figs.

This article contains such a large mass of statistical detail that only a few of the salient points can be given in an abstract. The figures are set out in 15 tables, 3 figures, 4 annexes and an addendum with 6 tables. Moreover, the patients are classified not only by age-groups but also by sex.

The investigation covered 43,078 patients over the years 1957 (20,221) and 1958 (22,857) treated in 148 clinics; the diseases concerned included gonorrhoea, syphilis and other conditions (chancroid, lymphogranuloma venereum and granuloma inguinale). Gonorrhoea increased by 2,691, syphilis fell by 57 and other conditions rose by 2 over the two years. The distribution of clinics was classified as (1) London (and its environs); (2) 5 cities with over 500,000 people; (3) 32 towns with populations 100,000-500,000; (4) 40 with 50,000-100,000; and (5) 45 with less than 50,000. More cases were treated in (1) than in (2), more in (2) than (3), and more in (3) than in (4); all areas showed an increase except (5); as regards age there was an increase in all groups in males except at 60 years and over, and in all females except at 40 years and

over; the peak prevalence in males was at 24-29 years and in females at 20-24 years; in females aged 15-19 infections rose from 22.6% to 23.5% of the whole incidence. As regards syphilis the female/male ratio changed from 1:4 to 1:3.5 and in gonorrhoea it remained at 1:3.7.

The increase in infections was most marked in young persons, most pronounced in males in London and pronounced in females both in London and in the larger cities.

T. E. Osmond

BRITISH CO-OPERATIVE CLINICAL GROUP [WILLCOX, R. R., Secretary.] **Country of Origin of Patients attending Venereal Disease Clinics: a Study of 138,626 Cases.** *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 233-42, 4 figs.

This article consists largely of tables and figures. An investigation was carried out on 138,626 patients who attended 105 clinics in England, Wales and Scotland in the years, 1952, 1955 and 1958; the clinics included 13 in Yorkshire, 20 in the North-West, 6 in the North-East, 18 in the West, 17 in London, 3 in the Midlands, 15 in South and East, 9 in Wales and 4 in Scotland. Patients included 37,818 with gonorrhoea and 100,808 with "other conditions".

In 1958 in males there were 7,930 from the U.K., 3,688 from the West Indies and 3,769 from other countries (including Asia, Mediterranean, Eire, West Africa, Europe, etc.); in females the corresponding figures were 2,709, 181 and 164. The percentage increases of gonorrhoea in males between 1952 and 1958 were: U.K. 17.3, West Indians 54.9 and others 27.8; in females the corresponding figures were 78.6, 14.7 and 6.7. In 1958 the proportion of male West Indian gonorrhoea patients varied widely in different regions, being 77.3% of the total patients in Huddersfield and over 45% in Birmingham, Ipswich and 3 of the London Clinics: the average was 40.3%.

As regards "other conditions" in 1958 in males, U.K. had 23,027, West Indies, 1,956, and other countries, 4,711: the corresponding figures for females were 8,536, 615 and 418.

It is concluded that in West Indians in 1958 the gonorrhoea rate per annum was at least 36.9 per 1,000 in males and 12 per 1,000 in females compared with 1.1 and 0.4 in U.K. patients.

There is a great deal more information in this article which can be obtained by a study of the original.

T. E. Osmond

TRICE, E. R. & CLARK, F. A., Jr., with the technical assistance of L. W. HINE, E. H. SHARPE & J. L. BYRD. **Transmission of Venereal Diseases through Homosexual Practices.** *Southern Med. J.* 1961, Jan., v. 54, No. 1, 76-9, 3 figs.

If, as has been stated, 37% of males indulge in homosexual practices, it is not surprising that the resultant incidence of venereal disease in, and caused by, these persons is high [NICOL, this *Bulletin*, 1960, v. 35, 779]. These authors report the case of a homosexual male

Negro found to have primary syphilis and acute gonorrhoea who named 10 contacts (7 males and 3 females); 4 of these males had syphilis; as a result 5 more patients were treated for gonorrhoea and 10 given prophylactic treatment.

In 1959, of 440 male patients at the Venereal Disease Clinic, Richmond, Virginia, 30 (7%) were homosexuals, and of 35 with early syphilis 20 (57%) were homosexuals. Another Negro with syphilis named 6 male contacts of whom 1 named 29 male contacts. Details of these 2 patients and their contacts are set out in 3 figures. As a result of this investigation 7 cases of primary, 4 of secondary and 10 of early latent syphilis were found, and in addition 20 males and 2 females were given prophylactic treatment.

2 cases of granuloma inguinale are recorded but the situations of the lesions are not given nor is it stated whether these occurred in the active or passive partner.

It is stated that rectal examination was not carried out where there was serological proof of syphilis and that Gram-stained smears were "unrewarding" [surely proctoscopic examination of the rectum and cultures where gonorrhoea is suspected should be the rule].

T. E. Osmond

VOGELSANG, T. M., PILLOT, J. & FAURE, M. Sérodiagnostic de la syphilis. Étude comparative des réactions "classiques" et de la fixation du complément avec l'antigène protéique du tréponème Reiter. [Serodiagnosis of Syphilis. Comparative Studies on "Conventional" Reactions and Complement Fixation with the Protein Antigen of Reiter's *Treponema*] *Ann. Inst. Pasteur.* 1961, Feb., v. 100, No. 2, 190-99, 1 fig. [24 refs.]

These authors compared classical serum tests for syphilis (STS) with complement-fixation tests with protein antigen obtained from the Reiter treponeme; this latter is an extension of the well known Pallida reaction of GAEHTGENS [this *Bulletin*, 1930, v. 5, 318, 724]. Two types of Reiter antigen were employed: (1) No. 27, washed organisms submitted to ultrasonic waves at pH 8 [see *ibid.*, 1960, v. 35, 993]; (2) No. 29, organisms treated with butanol and ether, then submitted to ultrasonic waves and the proteins purified by precipitation [*ibid.*, 1959, v. 34, 680]. The STS consisted of the Wassermann with cardiolipin antigen (B-W), the Meinicke and VDRL tube reactions. In all 1,078 sera, 677 from syphilitic persons and 401 from presumably non-syphilitic persons were tested in parallel. Of the former 63.9% were positive with B-W, 77.4% with Meinicke, 86.6% with VDRL, 78.4% with antigen No. 27 and 76.1% with antigen No. 29: the corresponding percentages with the non-syphilitic sera were 21.7, 41.9, 42.4, 17.6 and 15.6. Of the 677 syphilitic sera 80-90% gave concordant results with both types of test and the two Reiter tests agreed in 98.7%. With the non-syphilitic sera disagreement between STS and Reiter tests reached as high as 31.9% but the two Reiter tests agreed in 97.5%. One table shows results in various stages of syphilis comparing the two Reiter tests with one another and No. 27 with VDRL; in the latter agreement was 89.8%; most of the disagreements occurred in latent and treated cases.

Results show that the Reiter tests were equal in sensitivity and somewhat superior in specificity to the other reactions; No. 27 antigen appeared to be slightly superior to No. 29. It is concluded that the Reiter test is both simple and reliable.

[The number of positive reactions with presumably non-syphilitic sera appears to be very high with all tests. It would have been interesting to know more about the sources of these sera.]

T. E. Osmond

CARPENTER, C. M., MILLER, J. N., BOAK, Ruth A. & HEISKELL, C. L. The Relationship of *Brucella* Infection to Biologic False Positive Tests for Syphilis. *Amer. J. Med. Sci.* 1961, Feb., v. 241, No. 2, 231-4. [10 refs.]

The use of the *Treponema pallidum* immobilization (TPI) test has made it possible to evaluate the influence of different infections in producing biological false positive (BFP) results in the serological tests for syphilis (STS). Evidence of brucellar infection was obtained by performing brucella agglutination tests on 2,034 specimens of sera, and intradermal tests, with Brucellergen, an antigen obtained from *Brucella abortus*, on 278 patients. In this analysis persons whose sera were negative to both TPI and STS are considered as normal.

The authors found that *Brucella* agglutinins, ranging in titre from 1:20 to 1:5,120 occurred in 98 (21.1%) of 464 sera from patients with past or present syphilis, and in 327 (29.0%) of 1,126 sera from biological false positive reactors. Only 46 (10.4%) of 444 sera from normal subjects showed the presence of *Brucella* agglutinins. Dermal sensitivity to *Brucella* was recorded in 12 (36.4%) of 33 patients with present or past syphilis, in 21 (46.7%) of 45 patients with BFP reactions but in only 19 (9.5%) of 200 normal individuals.

It is concluded that there is an antigenic relationship between *Br. abortus* and *Trep. pallidum* and that in certain patients reagin formation may be due to infection with *Brucella*.

Frederick J. Wright

SEGAL, P., JANISZEWSKA-GELDNER, B. & LEONOWICZ-MICHNIOWSKA, J. Results of Penicillin Therapy in Syphilitic Primary Optic Atrophy. *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 257-60. [13 refs.]

There is nothing new in this article; many have reported their results in this condition, particularly MOORE (*Penicillin in Syphilis*, 1947, Oxford: Blackwell). The authors give their results in the treatment of 37 patients between 1950 and 1957; all had tabes or taboparesis and were observed for 3 to 6 years; ages in both sexes (26 men and 11 women) varied from under 40 to 59, most of the men being aged 51-59. Penicillin was used in a total dosage of 6 to 32 mega units and fever therapy in addition was used in 13 cases.

Patients were divided into 3 groups: (1) 16 were acute and the disease was arrested, (2) 16 were "deteriorating" and continued to do so in spite of treatment, (3) 5 were "inactive" and remained so.

Duration of the disease before the onset of deterioration of vision had no effect on the result, but the earlier treatment was started the better the outcome. Two types of cases were noted, one chronic and the other acute; the former offers the better prognosis, the latter progresses rapidly to permanent blindness in spite of treatment. [This appears to contradict what was said above for group (1).]

Technical details are set out in 7 tables.

T. E. Osmond

REYN, Alice, KORNER, B. & BENTZON, M. W. **Transportation of Material for the Culture of the Gonococcus.** *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 243-56, 2 figs. [55 refs.]

This article contains a large amount of statistical and other detail and as such should be studied in the original. Reyn *et al.* first discuss the experiences of numerous authors in their attempts to improve their methods in the cultural isolation of the gonococcus and then report their own findings. They employed 2 main media, the STUART [this *Bulletin*, 1946, v. 21, 620] and the McLEOD [*ibid.*, 1934, v. 9, 750]. The transportation media consisted of 1,000 ml. ox or veal meat both with 2% agar and 100 ml. defibrinated horse blood; the mixture was kept at 80°C. for 10 minutes and layers 1.5 cm. high were poured into tubes (15 × 150 mm.); these latter were later closed with cotton wool plugs soaked in paraffin. Culture medium consisted of a broth agar base of 1.8% agar in beef heart broth with 1% peptone, 0.3% NaCl and 0.2% Na₂HPO₄ · 12H₂O; this was melted, heated to 80°C. and 60 ml. defibrinated horse blood were added; after cooling to 56°C. 300 ml. of ascitic fluid were added and plates poured. 3 kinds of swabs were employed; wooden applicators boiled in phosphate buffer (1) with hydrophobic wool, (2) with hydrophilic wool, and (3) with hydrophilic wool impregnated with charcoal.

The "two methods of transporting gonococcus material" were called the Stuart and the McLeod and these were compared by using artificial and clinical material; temperature and time, gonococci and contaminants were considered. With Stuart's medium charcoal applicators proved superior, but not with McLeod's; the Stuart method preserved gonococci longer and showed fewer contaminants; in general growth was superior with specimens from males and with shorter transportation time; Polymyxin B sulphate inhibited *Escherichia coli*; the increase in agar concentration made for easier handling and tubes proved superior to stoppered bottles. In the result the Stuart method proved superior to the McLeod in the ratio of 12.4 to 8.5. T. E. Osmond

HARRIS, A., DEACON, W. E., TIEDEMANN, J. & PEACOCK, W. L., Jr. **Fluorescent Antibody Method of detecting Gonorrhea in Asymptomatic Females.** *Pub. Health Rep.* Wash. 1961, Feb., v. 76, No. 2, 93-6.

These authors examined 213 (162 Negro and 51 white) asymptomatic women, who were inmates of a women's prison, by means of the delayed fluorescent antibody

(FA) method. This consisted of taking swabs from the vagina, urethra and cervix; these were rotated in a chocolate agar slant and the tubes containing the swabs were placed in a candle jar at 35°C.; after 20 hours smears were made from the swabs, fixed with 3% formalin and stained with fluorescein-labelled gonococcus antiserum and examined by dark field with ultra-violet light.

Results showed 20.9% positives in Negroes and 19.6% in whites; all 3 sites gave positive results in 3 Negroes and 4 whites; for any 2 the figures were 10 and 3 and for 1 or more 50 and 21; vaginal specimens were positive in 20, cervical in 25 and urethral in 26. Re-examination of 74 patients after 7 days without treatment showed 4 positives in those negative at first and 6 negatives in those formerly positive. Of 30 patients re-examined 5-17 days after receiving 1.2 mega units of PAM only 1 showed gonococci.

It is concluded that the FA method is efficient and that repeat examinations are always indicated when the first is negative. T. E. Osmond

FITZGERALD, J. P. B. **The Oral Treatment of *Trichomonas vaginalis* Infestation.** *New Zealand Med. J.* 1961, Jan., v. 60, No. 341, 36-7.

After recording the experience of other authors [this *Bulletin*, 1961, v. 36, 146, *ter*] this author describes his own results with 23 patients. Treatment consisted of 200 mgm. of Metronidazole (RP 8823 Flagyl) given orally 3 times a day for a week: 21 were cured and 2 yielded to a second course; 6 husbands of the above who had no symptoms were also treated. Side effects were minimal and limited to nausea in 3 patients during the first 3 days of treatment. It is considered advisable to treat the sexual partners of all patients since the disease is often conveyed by intercourse. [In the summary 16 female patients are reported as having been cured.]

T. E. Osmond

DE ROM, R., THIÉRY, M., VAN SWIJNDREGT, L. M. & DASKALIDES, J. **Le Métronidazole. Chimiothérapie orale de la trichomonase vaginale. [Metronidazole Oral Chemotherapy of Trichomoniasis Vaginalis]** *Bruxelles-Méd.* 1961, Mar. 12, v. 41, No. 11, 349-55. [29 refs.]

In the past local treatment has frequently failed because the organisms have been hidden in the glands around the vagina; relapses have thus been frequent and reinfection from the sexual partner has been common. Metronidazole (Flagyl, 8823 RP) inhibits the growth *in vitro* of trichomonas in a concentration of 1/400,000 and is active in mouse infection.

These authors treated 79 patients by inserting a tablet of 500 mgm. into the vagina once a day for 20 days; a second group of 69 were treated systemically as well with 2 tablets each of 250 mgm. per day for 10 days. Tests of cure included 3 microscopical and cultural examinations. Male partners were treated orally only. Vaginal treatment gave 32% success and combined treatment 74%. In the first series the cure rate in 30

pregnant women for vaginal treatment was 27% and in 23 non-pregnant women 39%; in the second series success rates with combined treatment were 74% and 75% respectively.

Complications were mild, including local irritation, abdominal pain and some gastro-intestinal upset. In 58 patients treated during pregnancy there were 3 premature

births and 2 infant deaths (one of a premature baby delivered by Caesarean section, and one in a baby who died at 6 days, probably from an infection); neither of these was attributed to the drug.

Candida albicans occasionally appeared to increase but this was probably more apparent than real.

T. E. Osmond

GENERAL INFECTIVE DISEASES

The order in this section is:—General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.

GENERAL

DUBOS, R. G. *Health and Disease. J. Amer. Med. Ass.* 1960, Oct. 1, v. 174, No. 5, 505-7.

In this article the author, recently a recipient of the Passano Award, discusses the changes in the pattern of infectious disease which have occurred during the past 80 years. Pasteur's genius has been the main force in the study of infectious processes by bacteriological and immunological techniques which have had remarkable success in the control of bacterial and parasitic diseases. The view expressed, however, is that the "law of diminishing returns is beginning to operate in this approach to the problems of infection", and "the rewards in the future will not be commensurate with the effort and the cost". The power of classic techniques to discover effective agents in prophylaxis and therapy still exists provided there is enough time and money. "But I do question the magnitude of beneficial effects that we can derive from these techniques with regard to the total disease problem in our communities today." The types of infection which dominated 19th-century pathology "are becoming less destructive in our communities, but they are being replaced by other types of infectious processes which demand a reformulation of the germ theory". There are many reasons for the changed pattern of disease which lie not only in the success of medical techniques of control. "More important, probably, is the fact that changes in the genetic structure of the population and in the ways of life have altered considerably both the spread of infectious agents and our resistance to them." The modern study of infectious disease should not be based only on the search for effective methods of prophylaxis and therapy for it is probably more important to analyse the factors concerned in the "total environment" and the rapid changes which are occurring in our society and its ways of life. [See also this *Bulletin*, 1960, v. 35, 948.]

M. E. Delafield

FORBES, J. A. *Croup and its Management. Brit. Med. J.* 1961, Feb. 11, 389-92. [13 refs.]

This up-to-date review of croup and its management in young children from the Fairfield Infectious Diseases Hospital, Melbourne, is appropriate to the present viral and antibiotic age. The causal organism is now rarely *Corynebacterium diphtheriae* in countries with a high level of diphtheria immunization. During a period of 7 months 50% of 159 cases were proved to be due to *Myxovirus parainfluenzae* (types 1 and 3) during an epidemic, and type 2 (croup-associated virus) after the epidemic; more than half of the remainder were probably also viral in origin, and some 10% were due to, or aggravated by, bacterial infection. Additional viruses now known to cause the condition are influenza virus (types A and B), adenoviruses (types 1, 2, 3, 5, 7), measles virus, ECHO viruses (types 14 and 10) and Coxsackie virus (type A9). A non-infectious form of the disease (anaphylactoid laryngeal oedema) occurs more rarely.

Clinically, supraglottic oedema (influenzal epiglottitis) should be distinguished from acute laryngotracheobronchitis. The rounded oedematous red epiglottis may be seen as a "gagging", or felt by the palpating finger; when this condition is progressive, tracheotomy is usually indicated.

The general management, apart from specific treatment, is the same as for diphtheritic cases—a steam tent, avoidance of oxygen and sedation, and tracheotomy in progressive cases exhibiting costal retraction, restlessness, fatigue, and cyanosis. Antibiotics are used to suppress or treat secondary bacterial infection, and in all severe cases, including those of supraglottic oedema, chloramphenicol is the most effective drug. Bronchoscopy is contra-indicated in such an acute condition. The technique and management of tracheotomy are much the same as for obstructive laryngeal diphtheria.

H. Stanley Banks

POOL, J. H., WALTON, J. N., BREWIS, E. G., ULDALL, P. R., WRIGHT, A. E. & GARDNER, P. S. *Benign Myalgic Encephalomyelitis in Newcastle upon Tyne. Lancet.* 1961, Apr. 8, 733-7, 1 fig. [13 refs.]

This is a description of an outbreak of benign myalgic encephalomyelitis which occurred in a training college

for young women in Newcastle upon Tyne in the autumn of 1959. There were 48 cases, 26 mild, 12 moderately severe and 10 very severe. The mild and moderately severe cases would possibly have been diagnosed as influenza but for their association with the severe cases in whom neurological features were prominent. The clinical picture was very similar to that occurring in "Royal Free disease" in 1955 [this *Bulletin*, 1958, v. 33, 16] and in illnesses reported in other parts of the world, notably Iceland and Durban. There were marked emotional lability, often resembling hysteria, and gross muscular weakness and incoordination with minimal neurological signs. Laboratory investigations were negative.

A. B. Christie

PRICE, J. L. *Myalgic Encephalomyelitis*. *Lancet*. 1961, Apr. 8, 737-8.

The author describes the illnesses of 2 female patients, aged 37 and 20, in whom the main symptoms were difficulty in initiating movements, tremor on voluntary movement, rapid muscular fatigue and emotional lability. Both patients developed respiratory embarrassment requiring treatment in a tank respirator. Laboratory investigations were negative. The symptoms were typical of benign myalgic encephalomyelitis. The patients had no contact with each other or with any other known cases. The author feels that the condition probably occurs sporadically more often than is generally realized.

A. B. Christie

PÁLFFY, G. & MEREI, F. T. *The Possible Role of Vaccines and Sera in the Pathogenesis of Multiple Sclerosis*. *World Neurology*. Minneapolis. 1961, Feb., v. 2, No. 2, 167-72. [20 refs.]

The authors reviewed 139 cases of multiple sclerosis treated at the Pécs Medical School, Hungary, between 1949 and 1959: they found 8 instances of apparent relationship between the administration of sera or vaccines and the onset or aggravation of multiple sclerosis. They feel that such cases lend support to the theory of neuroallergic origin of the disease and that vaccines and sera should be administered to patients already suffering from multiple sclerosis only in cases of utmost necessity.

A. B. Christie

MENZIN, A. W. *Current Immunization Methods and Materials. A Review*. *Arch. Intern. Med.* 1961, Mar., v. 107, No. 3, 409-29. [23 refs.]

HOSPITAL AND OTHER CROSS INFECTIONS

J. CLIN. PATH. 1961, Jan., v. 14, No. 1, 1-98, illustrated. [Numerous refs.] A Special Issue in Honour of Leonard Colebrook for his Pioneer Work on Hospital Cross-Infection.

The whole of the January 1961 number of the *Journal of Clinical Pathology* is devoted to papers on various aspects of hospital infection, the number being dedicated to Leonard COLEBROOK. A particularly useful feature of many of the papers is the provision of details of the proprietary preparations mentioned.

Mary BARBER (*Hospital infection yesterday and today*, pp. 2-10), after a brief historical introduction, discusses the information available on the incidence of infection and on the extent to which antibiotic resistance has developed in various bacteria. She also stresses the current importance of infection with Gram-negative bacilli.

R. KNOX contributes *A survey of some problems in sterilization* (pp. 11-17), in which he discusses briefly the modern developments in heat sterilization and then raises, and to some extent answers, a series of questions. These include: When is sterilization necessary? How, where, and how often, should it be done? How is the effectiveness of a sterilizing process to be judged? Knox emphasizes that, not only must the sterilizing methods be matched to the materials to be treated, but the whole organization may need to be different for different equipment: for some material sterilization by industrial processes has great advantages over anything the hospital can do, and this needs to be remembered in hospital planning.

R. BLOWERS (*Control of infection in hospital wards*, pp. 18-25) describes a number of preventive measures in some detail. He lists the conditions held to justify isolation of an infected patient and the various methods of achieving it. He then describes methods for the control of bacterial contamination of the ward and its equipment. The difficulty of making proper tests of control methods is stressed, as is the need for attempting them.

Chemical disinfection in the prevention of infection in hospital is discussed by W. A. GILLESPIE (pp. 26-31). After the initial success of locally applied disinfectants in obstetrics and burns, the method has proved of great value in preventing sepsis among infants in maternity hospital, and as a supplement to asepsis in the prevention of post-operative urinary tract infection. In surgical wards chemical disinfectants are being used for the prevention of nose and skin carriage of staphylococci by patients and staff and as a topical spray to the wound.

In The cleaning of ward floors and the bacteriological study of floor-cleaning machines (pp. 32-37) J. G. BATE gives a useful brief summary of the floor materials available and of various floor cleaning methods. He also illustrates the method used for testing the bactericidal retention of vacuum cleaners [see also this *Bulletin*, 1961, v. 36, 478].

Sterilization by dry heat is reviewed by E. M. DARMADY, K. E. A. HUGHES, J. D. JONES, D. PRINCE and Winifred TUKE (pp. 38-44). Hot-air ovens are the most popular of the methods but have a number of disadvantages. For a large syringe service, the conveyor-belt infra-red sterilizer has proved very useful; for a smaller number the heated aluminium block is satisfactory. A new method, depending on the use of infra-red in a high vacuum, has been developed for rapid sterilization of instruments and can sterilize in 10 minutes. The time and temperature noted for dry heat sterilization are discussed.

R. A. SHOOTER and R. E. O. WILLIAMS (*Prevention of infection in operating theatres*, pp. 45-48) emphasize the need for maintaining specific records if the incidence of sepsis is to be ascertained, and then survey the sources of infection in theatres—staff with septic lesions, carriers, the air, the patient himself, and unsterile material. The last source is more important for clostridial infections and urinary tract infections than for staphylococcal sepsis.

J. W. HOWIE opens his paper on *The surgeon's autoclave* (pp. 49-54) with a forthright assertion that all the apparatus used to sterilize surgical material should render it free of living micro-organisms. He then discusses the importance of a clear chain of responsibility for the management and testing of the autoclave. The steam requirements, and the times advised for sterilizing loads at different temperatures are stated. On the testing of autoclaves, the primary need is for an engineer's investigation; bacteriological tests have only a secondary place.

In *Radiation sterilization* (pp. 55-58) E. M. DARMADY, K. E. A. HUGHES, Margaret M. BURT, Barbara M. FREEMAN and D. B. POWELL report a number of tests of the ability of gamma rays to sterilize various preparations of vegetative and spore-bearing organisms. 2.5 mega rad produced complete sterility in all tests. Some preparations of *Bacillus pumilus* and of *Clostridium welchii* survived 1.5 or 2.0 mega rad.

A brief but valuable paper on *Sterilization by ethylene oxide* by J. C. KELSEY (pp. 59-61) outlines the many difficulties in defining satisfactory disinfecting conditions for the use of the agent.

In *Sterilization by gas ovens* by E. A. K. PATRICK, R. H. WHARTON, K. PRENTIS and A. G. SIGNY (pp. 62-65), 2 continuous-flow syringe sterilizers are described in which gas is used as the source of heat. 1 could deal with 500 syringes per hour with a gas consumption of 1.3 therms per 1,000 syringes.

A variety of unsatisfactory methods for the *Disinfection of bedpans* are mentioned by E. M. DARMADY, K. E. A. HUGHES, J. D. JONES, D. PRINCE and Patricia VERDON (pp. 66-68) who then describe the use of a modified crockery washing machine in which the sluiced pans are heated to 180°F. in water.

The organization of central sterile supply departments is reviewed by J. D. WELCH (pp. 69-75). He considers that these departments aim to improve the standard of hospital sterilizing and to provide a more efficient service than can otherwise be achieved. Dressings and other "soft" supplies are best made of disposable materials as far as possible and packed in paper or cardboard boxes. Instruments can conveniently be packed in extruded aluminium tubes (as used for syringes), if scissors, etc., are made to open out fully. Disposable syringes are unlikely to be economic in the near future but disposable hypodermic needles are economic [and are now available in Britain]. Of the methods for distributing equipment from the store the requisition list has been found the most convenient.

V. G. ALDER and F. I. ALDER (*Preserving the sterility of surgical dressings wrapped in paper and other materials*, pp. 76-79) report some experiments on preventing the recontamination of sterilized dressings stored in various wrappings. Crêpe paper was satisfactory, especially if protected by a cardboard box.

A paper by I. M. LARKIN, E. Y. BRIDSON, W. S. M. GRIEVE and J. W. GIBSON (*Disinfection of hospital blankets with Synthetic Phenolic Compounds*, pp. 80-84) describes laboratory and pilot laundry tests of Hycolin (a mixture of halogenated alkyl/aryl phenols) for the disinfection of blankets by immersion during the laundering process. The advantage claimed for this substance is its ability to kill *Ps. pyocyanea* and *Myc. tuberculosis* as well as Gram-positive cocci and coliform organisms. The dipped blankets are best dried in a hot-air dryer.

E. J. L. LOWBURY contributes a valuable paper on *Skin disinfection* (pp. 85-90) in which he recalls earlier work, distinguishes the various requirements for skin disinfectants, and summarizes his own work on various agents. [See also this *Bulletin*, 1951, v. 26, 712; 1960, v. 35, 1223; 1961, v. 36, 179.]

P. E. VERDON reports a series of *Efficiency tests on a series of common skin antiseptics under ward conditions* (pp. 91-93) in which the reduction in the normal flora of the antecubital fossa was estimated by a replica plating technique. "Laurolinium" [the composition of which is not stated] was found to give the best results and was significantly better than alcohol, iodine in alcohol, cetrimide with hibitane, merthiolate tincture, Roccal, etc.

J. BRADLEY and M. J. MEYNELL give a brief report of *A survey of staphylococci isolated in hospital practice* (pp. 94-95). Of 492 strains from one casualty department 4.5% were phage-type 80 and 61.5% were sensitive to penicillin. For 500 strains from in-patients the proportions were 10.0% and 23.4%.

O. WESLEY-JAMES and V. G. ALDER examined *Staphylococci in septic fingers* (pp. 96-98) and compared the phage types with those of staphylococci from the noses of the patients and of others. The lesions yielded a higher proportion of type 80 and 52A/79 strains. In many cases strains of the same type were found in nose and lesions. Severity of lesions seemed to vary with phage type.

R. E. O. Williams

SCHMIDT, J. Untersuchungen zur Frage des latenten Staphylokokken-Hospitalismus. [Investigation of Latent Staphylococcal Hospital Infection] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 1, 359-63. [18 refs.]

The English summary appended to the paper is as follows:—

"The occurrence of a latent staphylococcal hospital germ is reported. 28.8 per cent of specimens taken from patients, staff members, items and air of the ward rooms yielded a penicillin resistant staphylococcus strain of the phage pattern 6/7/53/77, giving a negative yolk test. This strain was never isolated from a case of staphylococcal infection; 69.1% of the mastitis cases were caused by a penicillin resistant, yolk-test-negative staphylococcus strain of the phage pattern 52/(52A 79)/80. The latter strain showed significantly higher α -haemolysin titers than the avirulent strain, however, the mean difference was one dilution step only. The avirulent strain proved to produce more hyaluronidase than the strain isolated from pathological processes."

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus*, *Streptococcus*, *Neisseria*, *Others*.

RAVITCH, M. M. & FEIN, R. **The Changing Picture of Pneumonia and Empyema in Infants and Children. A Review of the Experience at the Harriet Lane Home from 1934 through 1958.** *J. Amer. Med. Ass.* 1961, Mar. 25, v. 175, No. 12, 1039-44, 1 fig.

The authors review the changing picture of pneumonia and empyema in children from 1934 to 1958 in the Harriet Lane Home, Johns Hopkins Hospital, Baltimore. Altogether there were 10,632 cases of pneumonia and 214 cases of empyema. Antibacterial therapy has decreased the need to admit to hospital children suffering from pneumonia and has almost eliminated the incidence of empyema due to pneumococci, streptococci and *Haemophilus influenzae*. On the other hand, there has been a sharp rise in staphylococcal empyema, almost entirely in infants.

A. B. Christie

OLESEN, K. H. & QUADE, F. **Pneumothorax accompanying Staphylococcal Pneumonia in Patients treated with Steroids.** *Lancet*. 1961, Mar. 11, 535-6. [10 refs.]

The authors record the occurrence of pneumothorax in 4 patients suffering from staphylococcal pneumonia and treated with antibiotics and steroids: the ages were 3½, 9, 15 and 23 years. In examining the records for the distribution of pneumothorax in patients treated in the Blegsdamhospitalet, Copenhagen, in 1958-59, the authors found 4 cases of pneumothorax in 19 patients suffering from staphylococcal pneumonia and treated with cortisone but none in 26 patients not treated with cortisone: in 200 patients suffering from other conditions and treated with cortisone there were 3 cases of pneumothorax and in 7,272 patients, not given cortisone, also 3 cases. In the 4 cases cited, the pneumothorax caused no symptoms and the authors feel that, even if steroids are not a contributory cause of pneumothorax, they certainly mask the symptoms.

A. B. Christie

ABBOTT, Mary I. & RILEY, H. D., Jr. **Treatment of Staphylococcal Infections in the Young Infant with Tetracycline and Novobiocin in Combination.** *Antibiotic Med.* New York. 1961, Jan., v. 8, No. 1, 23-8. [17 refs.]

During an outbreak of staphylococcal infection in a nursery, 28 infants were treated orally with a combination of 2 parts tetracycline to 1 part novobiocin: dosage ranged from 12 to 25 mgm. per lb. body weight daily but in the more serious cases doses of up to 70 mgm. per lb. daily were given. 21 infants were suffering from pyoderma only, 3 had staphylococcal septicaemia, 2 staphylococcal pneumonia and 2 had streptococcal omphalitis. 1 of the infants with pneumonia and 1 with omphalitis failed to respond: in all the others the clinical

response was satisfactory. There were no controls though the authors state that a significant number of other infants treated differently developed serious complications. The authors refer to other work on similar antibiotic combinations but do not claim that their own results prove anything regarding synergism.

A. B. Christie

RASKA, K. **Epidemiologie streptokokových nákaz a jejich následků. [Epidemiology of Streptococcal Infections and their Sequelae]** *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 2, 73-91, 7 figs. [42 refs.]

The English summary appended to the paper is as follows:—

"1. The author gives a short survey of the present knowledge of epidemiology of streptococcal infections and their sequelae.

"2. In Czechoslovakia, there exists a high morbidity on scarlet fever up to the present time (235.6 per 100,000, in 1959). After the treatment with penicillin was introduced with a short-time 6 day hospitalization, in 1949, an enduring and radical decrease of complications as well as sequelae of the scarlet fever resulted. The number of repeated cases of scarlet fever has grown unusually high. Almost one-fifth of all hospitalized cases are patients who fell ill twice or even more times.

"3. Immunological surveys concerning the findings of antistreptolysin O in different age groups of the population may afford valuable information about the recent exposition to streptococcal infections.

"4. Rheumatic fever and rheumatic heart diseases represent amongst diseases of cardiovascular system 6.2 p.c. of all causes of death, in Czechoslovakia.

"5. The study of the morbidity in selected districts as well as the activities of the dispensaries for cardiac and vascular diseases in children show, in comparison with some other countries, relatively high numbers of incidence and prevalence of rheumatic fever and of rheumatic heart disorders in Czechoslovakia.

"6. During the last years, an effort has been developed on the basis of dispensaries for cardiac and vascular diseases of children, which are built all over the state, in preventing rheumatic fever, too.

"7. Streptococcal infections and their delayed sequelae still represent an important health problem, in Czechoslovakia. Some facts presented in the paper show the direction of the further studies of these questions."

HAMBURGER, M., KAPLAN, S. & WALKER, W. F. **Subacute Bacterial Endocarditis caused by Penicillin-Sensitive Streptococci. Value of Oral Phenoxymethyl Penicillin and Intramuscular Streptomycin.** *J. Amer. Med. Ass.* 1961, Feb. 18, v. 175, No. 7, 554-7. [20 refs.]

The authors treated 17 patients suffering from subacute bacterial endocarditis due to penicillin-sensitive streptococci with phenoxymethyl penicillin and streptomycin. The dose of penicillin varied from 500 to 750 mgm. every 4 hours: the dose of streptomycin was 1 gm. every 12

hours for adults, and 0.5 mgm. for children; treatment was continued for 14 to 15 days. All patients recovered and were followed up for 6 to 54 months: 3 died during the follow-up period, 1 from burns, 1 from cardiac failure and 1 from unknown cause. *A. B. Christie*

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

PETRONE, P. Considerazioni statistiche sulla vaccino-profilassi della difterite e suggerimenti d'indole tecnico-organizzativa per una sistematica e piu' efficiente profilassi di massa. [Statistical Considerations on Diphtheria Immunization and Technical and Practical Suggestions for a Systematic and More Efficient Mass-Prophylaxis] *Ann. d. San. Pubblica.* Rome. 1960, Nov.-Dec., v. 21, No. 6, 1523-9. [16 refs.] English summary.

Petrone touches briefly on the history of diphtheria and refers to the development and results of immunization in various countries. He tabulates the annual number of cases and incidence rates recorded in Italy during 1930-58 and compares his country's figures, unfavourably in 6 out of 8 cases, with those reported from other countries where immunization against diphtheria has also been compulsory for some years. In a 1929 circular, the Italian authorities first urged that all children should be inoculated against the disease, and such immunization was made compulsory in 1939-40.

The author gives the number of cases of diphtheria which were reported in each of the 10 years 1950-59 for the Province of Potenza, and the corresponding number of patients isolated in the Provincial Hospital; the latter has risen progressively from 14 to 41. Diphtheria still accounts for a death-rate of 1.8 per 10,000 and it is obvious that the law is not being adequately complied with or sufficiently enforced in the matter of immunization. The Italian public, and some members of their medical profession, have yet to appreciate the full social value of anti-diphtheria inoculation.

It is suggested that (1) an identity health card should be issued for every child at the time of birth notification, (2) preventive inoculations should be given in health offices, school clinics and, if requested, at home by health department personnel who have been specially trained, (3) the number of injections should be cut down as far as possible by the use of mixed vaccines, and (4) more local health offices, with adequately trained staff, should be set up to ensure easy access by every village community. *J. Cauchi*

WHITAKER, Jo Anne, NELSON, J. D. & FINK, C. W. The Fluorescent Antitoxin Test for the Immediate Diagnosis of Diphtheria. *Pediatrics.* Springfield, Ill. 1961, Feb., v. 27, No. 2, 214-18.

It is claimed that a reliable and rapid diagnosis of diphtheria can be effected within an hour if smears from the throat or other affected mucous membrane are treated with a preparation of highly purified diphtheria antitoxin in which the globulin has been conjugated with isothiocyanate. After exposure to the fluorescein-conjugated antibody for 30 minutes the slides are washed and then mounted in glycerin and examined with dark-field condenser using a mercury arc lamp as source of light and suitable filters.

8 out of 9 frank clinical cases of diphtheria gave positive results; with one exception all controls, 89 in number and including cases of pertussis and of non-diphtheritic membranous tonsillitis, were negative. The exception was a case of streptococcal pharyngitis and it is suggested that the patient was also a carrier of toxigenic *Corynebacterium diphtheriae*.

Staining of preparations from cultures of toxigenic *C. diphtheriae* shows many negative as well as positive bacteria and it is assumed that only some of the bacteria in any preparation are active in toxin production at any one time.

Considerable delay in the examination of preparations after they have been taken from the patient leads to negative results. So also does antitoxin treatment if it has been in progress for some time.

[Provided the results are confirmed in larger groups of clinical cases and are found to be positive with all types of *C. diphtheriae* infection the method should be of great value. The diphtheria investigated was apparently severe as 2 of the 9 cases recorded were fatal.]

J. W. McLeod

VYSOKÁ-BURIANOVÁ, B., with the assistance of J. RADKOVSKÝ & M. CHODĚROVÁ. Imunologický přehled výskytu protilátek proti pertusi a parapertusi v některých krajích ČSSR. [An Immunological Survey of the Prevalence of Antibodies against Pertussis and Parapertussis in some Regions of Czechoslovakia] *Českoslov. Epidemiol., Mikrobiol. & Imunol.* Prague. 1960, v. 9, No. 8, 523-34, 5 graphs. [13 refs.] English summary.

An investigation has been made of the incidence and age distribution of agglutinins to *Haemophilus [Bordetella] pertussis* and *H. [B.] parapertussis* in 5,770 sera of inhabitants of the areas of Prague and 4 other large towns of Czechoslovakia. In Prague *H. pertussis* antibody was already present in the 3rd year of life in 40% of sera examined, whereas in the other areas the proportion of sera with antibody did not reach 15-20% until the 10th year. *H. parapertussis* antibody did not appear until the 3rd year of life and in Prague reached a maximum incidence of 50% at the 10th year. *D. J. Bauer*

ROSENTHAL, A., NETER, E. & WEPPNER, D. F. Recovery from *Salmonella* Meningitis after Treatment with Furaladone (Altafur). *J. Pediatrics.* St. Louis. 1961, Mar., v. 58, No. 3, 377-80, 1 fig.

"Apparent successful therapy with furaladone, administered intravenously, of an infant with *Sal.*

schwarzengrund meningitis is described. The patient had failed to recover from the infection after previous treatment with several antibiotics. Furaladone was tolerated rather well."

KOPACKA, Bronisława, ŁUKAWSKA, Halina & ŚLUBICKA, Anna. Badania serologiczne i bakteriologiczne w wykrywaniu nosicielstwa durowego. [Serological and Bacteriological Investigations in detecting Typhoid Fever Carriers] *Med. Dośw. i Mikrob.* Warsaw. 1961, v. 13, No. 1, 1-13. [23 refs.]

The English summary appended to the paper is as follows:—

"Studies were carried out on the antigens for Vi agglutination and hemagglutination. The diagnostic value of antigens was checked on animal and human immunity sera.

"As a result of the undertaken investigations it was found that the most sensitive, specific and stable antigen for Vi agglutination reaction proved to be the suspension from *S. typhi* 6S strain, obtained after Ando and Shimojo method, from antigens for Vi hemagglutination—'crude' antigen prepared from *S. typhi* 6S strain in the solution of physiological salt and lyophilized. 'Crude' Vi antigen proved to be serologically pure preparation of Vi without the admixture of somatic antigen. This is important from the point of view of sero-diagnostics of the carrier-state since in Poland because of the yearly universal vaccination by means of typhoid endotoxin a high percentage of the population possess post-vaccination somatic O antibodies.

"The antigens prepared were employed in serological investigations of 122 carriers who were simultaneously under bacteriological control. In 83 bacteriologically positive carriers confirmation was found in 92.7% in Vi hemagglutination reaction and in 85.5% in Vi agglutination reaction considering as positive titres from 1:40 in hemagglutination and from 1:20 in agglutination. This level of titres of diagnostic importance has been accepted by the authors on the basis of control examination: out of 133 individuals, in 5 the titres found were from 1:40 to 1:160 in Vi hemagglutination reaction, in 6 individuals titres were from 1:20 to 1:160 in Vi agglutination reaction, and negative and lower titres than those mentioned were found in 96.3% in hemagglutination reaction and 95.5% in agglutination reaction.

"In the group of 39 bacteriologically negative carriers in whom typhoid bacilli were not detected during the period of the last 1-2 years, negative Vi hemagglutination reaction or low titres without diagnostic significance were found in 30 individuals. Majority of these individuals were cancelled from the files of carriers. 9 cases however present positive Vi hemagglutination titres and in 12 cases positive Vi agglutination titres and therefore they still remain for further control.

"In conclusion Vi serodiagnostics is a valuable method of carrier control. It does not, however, detect 100% of carriers and therefore cannot be the only method of detecting the carrier-state."

MAIN, R. G. Treatment of the Chronic Alimentary Enteric Carrier. *Brit. Med. J.* 1961, Feb. 4, 328-33, 1 chart. [Numerous refs.]

As a result of an episode of acute cholecystitis in a chronic carrier of *Salmonella paratyphi B* in a mental hospital, cholecystectomy and *choledochostomy* were performed, and after a period of 4 months the stools became persistently negative. The surgeon then became interested in a group of 8 chronic carriers of *Salm. paratyphi B* in the hospital (one of whom was also an intermittent carrier of *Salm. typhi*). He performed cholecystectomy on all of these, followed by a course of oral neomycin; in 7 of them the carrier state was apparently eliminated within 2 months—an observation based on approximately 2 years' observation. The remaining carrier relapsed after 4 months. He had been one of the most constant faecal excretors; at operation the bile duct had been found to be dilated and had been drained by a T-tube; after operation his serum bilirubin level had fluctuated and shown a tendency to rise; his erythrocyte sedimentation rate, alone of the 9, remained significantly elevated; and he alone retained after operation a positive O titre for *Salm. paratyphi B*. These are probably signs of continuing infection. An intravenous cholangiogram showed the common bile duct to be still dilated and also blocked near the entrance to the duodenum.

A second operation on this carrier showed blockage at the sphincter opening of the duct, and choledochal sphincterotomy was performed, and the duct drained again with a T-tube. This was successful; stool cultures have remained negative for 17 months.

[This interesting report should be considered along with that of ERLIK and REITER (this *Bulletin*, 1960, v. 35, 1115). These workers in Israel advocated drainage of the bile duct in all cholecystectomy operations in typhoid carriers. The time seems to have come for a reconsideration of the surgery of the chronic typhoid carrier. The condition is potentially dangerous (and always irksome) to the carrier as well as to the community. There seems now to be presumptive evidence that cholecystectomy combined with adequate drainage of the biliary ducts may be highly successful in eliminating the carrier state.]

H. Stanley Banks

NICHOLSON, F. & MASI, A. T. Experience with Enteropathogenic *E. coli*, *Shigella*, and *Salmonella* in Infants and Young Children in St. Thomas, Virgin Islands. *Bol. Asoc. Med. de Puerto Rico*. 1960, Oct., v. 52, No. 10, 323-30. [14 refs.]

This is a report on the bacteriological examination of the stools of 1,000 infants and young children with diarrhoea, as seen over a period of 3 years in the Knud-Hansen Memorial Hospital, St. Thomas, which is one of the chief of the islands in the Virgin group belonging to the United States of America. Of the 1,000 patients, 468 were recorded as cases of gastro-enteritis while the remaining 532 suffered from diarrhoea only without any constitutional disturbances. From the stools of the patients with gastro-enteritis enteropathogenic *Escherichia coli* were isolated from 58, shigellae from 43 and salmonellae from 8. Of the 58 *E. coli*, 29 were identified as

E. coli O 111 and there is some indication that a proportion of these could be regarded as hospital cross-infections. Of the 43 shigellae, 28 were identified as *Shigella flexneri* 2 and 11 as *Sh. sonnei*. It is reported that all the specimens from 532 patients suffering from diarrhoea without pyrexia or signs of vomiting were negative for enteropathogenic *E. coli*, *Shigella* or *Salmonella*.

In the absence of any information about the general and social conditions of the patients, incidence of diarrhoeal diseases and other relevant information about the health of the general population of the island (apart from the fact that *Sh. flexneri* had been isolated from a case of bacillary dysentery in 1956, before which this organism had not been isolated for 10 years) it is difficult to comment on these rather unusual findings.

H. J. Bensted

ROGERS, K. B. & TAYLOR, Joan. **Laboratory Diagnosis of Gastro-Enteritis due to *Escherichia coli*.** *Bull. World Health Organization*. Geneva. 1961, v. 24, No. 1, 59-71. [Numerous refs.]

This is essentially a practical article by two of the most experienced workers on infant gastro-enteritis. It describes very clearly the routine methods to be followed by the clinical pathologist in dealing with an outbreak of gastro-enteritis in infants where the cause is suspected of being one of the enteropathogenic *Escherichia coli*.

After a brief historical introduction dealing with the emergence of the aetiological importance of certain strains of *E. coli* in epidemic infant gastro-enteritis there are short sections on the management of outbreaks, collection of specimens and the laboratory examination of the stool samples. Finally there is a section on the media and reagents used in the cultural and biochemical tests. Although the authors draw largely on their own very extensive experience, consideration is given to the work of others and the article is well documented.

There are descriptions of the naked-eye appearance of infants' stools under varying conditions. Intestinal protozoa may be associated with infant gastro-enteritis [especially in areas bordering on the eastern Mediterranean where the flagellate *Giardia intestinalis* may be very common; this protozoon is by no means limited to that area—it is found sometimes in nursery outbreaks in Great Britain].

The general antigenic structure of the enteropathogenic *E. coli* is discussed but, wisely, no attempt is made to consider in detail individual types, the finer differentiation in accordance with their H antigens or the peculiar surface antigens associated with this group. The methods recommended for serological identification of the enteropathogenic *E. coli* isolated from patients with gastro-enteritis are simple agglutination tests with sera containing the specific O-antibody complex of the various accepted types. It is understood that such sera would be generally available from a central laboratory as they are in Great Britain and that for any further investigation required for epidemiological studies or other purposes the cultures would be forwarded to a suitable reference laboratory.

[This is a straightforward and valuable article, which keeps well within its terms of reference.] H. J. Bensted

DA MOTTA, L. A. C. R. C. **Epidemiology of Human Brucellosis in Portugal with consideration of some of its Economic and Social Aspects.** *Anais Inst. Med. Trop.* Lisbon. 1959, Jan.-Dec., v. 16, Nos. 1/4, 305-406, 2 folding maps & 7 graphs (1 folding). [125 refs.]

This is an admirable account of the epidemiology of human brucellosis in Portugal which is clearly written and interesting to read. It is preceded by an introduction devoted to a brief history of brucellosis in the world; its aetiology; reservoirs of infection; methods of transmission; immuno-allergy; medical, social and economic aspects of the disease and international action which has been taken for its study and control. All human cases in Portugal have so far been proved to be due only to *Brucella melitensis*.

In Portugal human brucellosis has been known under a variety of names for centuries. The National Public Health Department have since 1913 sponsored surveys and investigations the most important of which was the survey of 1950 which followed the introduction of compulsory notification of human brucellosis in that year. This survey revealed that the incidence of typical clinical cases only, as an average over the previous 5 years, was 12-13 per 100,000 and also that raw goat's milk and the fresh cheese made from it appeared to be the main, if not the only, source of infection to man. These results led to the creation, also in 1950, of a National Commission for the Study of Brucellosis of which the author was a junior medical member. There is a good account of the findings of this commission and of other investigations which have led to control measures particularly against caprine brucellosis, prophylactic measures mainly of health education and to free treatment of poor patients. These measures have had appreciable though only partial success. Sections of the report contain detailed descriptions and discussions of morbidity, mortality rates, aetiology, sources of infection, geographical distribution and incidence by season, sex, age and occupation. There are a considerable number of numerical tables, maps and graphs. Long, detailed summaries in English, Portuguese and French are appended.

Much remains to be done to control and prevent human brucellosis in Portugal but considerable progress has already been achieved.

M. E. Delafield

JANTAFFI, C., PROVVIDENZA, G., AVELLA, A. & CALVANI, M. **Indagini epidemiologiche e cliniche su 245 casi di brucellosi ricoverati dal 1949 al 1958. Nota II—(Indagini cliniche—Trattamento).** [Epidemiological and Clinical Investigations on 245 Cases of Brucellosis Admitted from 1949 to 1958—2nd Note (Clinical Investigations—Treatment)] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Dec., v. 41, No. 12, 625-32. English summary (4 lines).

The authors tabulate the distribution of signs and symptoms among their 245 patients. Pyrexia was present in all but the temperature curve was not always characteristic. There was no appreciable enlargement of the spleen in 18, and the liver was enlarged in 218 patients.

Van den Bergh and other tests confirmed that the hepatic function was involved in a proportion of the latter.

Every patient gave a positive blood serum test, from 10 days to 5 months after onset, at titres varying between 1 in 200 and 1 in 10,000. The reaction was to *Brucella melitensis* in 176 patients, to *Br. abortus* in 21 and to both species in 52.

Of the 2 patients who died, one had developed a pulmonary abscess and the other was already seriously ill when admitted and he died a week later.

Antibiotic drugs had not yet become available for the first 25 patients in this series and they were treated with *Br. melitensis* vaccine alone. The remainder were given vaccine as well as a variety of antibiotics, singly or in combination. A table is given to show the number who received each type of treatment and the limits of time which each such treatment took to bring down the pyrexia. Cortisone was also given to 11 of the patients.

The vaccine was injected intravenously in progressive doses rising from 5 to 400 million organisms, or intramuscularly progressing from 100,000 to 2,000 million *Brucella*, repeated every 4-8 days and continued for 18-29 days after the fever.

The authors prefer a combination of vaccine with either tetracycline and streptomycin or chloramphenicol and streptomycin.

J. Cauchi

SZMUNESS, W. & PARNAS, J. Aspects particuliers de l'épidémiologie de la brucellose humaine en Pologne. [Epidemiology of Brucellosis in Man in Poland] *Arch. Inst. Pasteur de Tunis*. 1960, Dec., v. 37, No. 4, 457-84, 9 figs.

Human brucellosis is not a notifiable disease in Great Britain and official figures of its incidence in this country are not available as they are for many other countries. It is not known how the quoted figures for incidence of the disease in other countries were obtained or what methods of diagnosis are acceptable for notification, but in view of the caution that must always be exercised in diagnosing brucellosis in the absence of a positive blood culture or an unquestionable serological reaction with a significant agglutinin response, it is difficult to assess the comparative value of the figures quoted. Nevertheless it would seem reasonable to accept the fact that brucellosis in Italy with a declared incidence of 10-20 per 100,000 of the population is a more important disease than it is in Poland where the declared incidence is in the region of 0.4 per 100,000 of the population.

This paper contains a good deal of detailed information about the incidence of human brucellosis in the various administrative areas in Poland, relating raised incidences to local animal brucellosis and also setting out the occupations, sex and age-groups of the persons who were reported to be infected. As would be expected the majority of the human infections were found in adult males who were in direct contact with farm animals, particularly those concerned with the birth of calves on farms. All such persons were considered to be at greater risk than those, not in direct contact with these animals, who drank raw milk rather than heat-treated milk. No information is given about the extent of the heat-treatment of milk in Poland and this article is mainly

concerned with the ultimate problem of the eradication of brucellosis, as an animal disease, rather than the immediate problem of the safety of milk for human consumption.

The paper does not disclose any new information but it makes quite interesting reading. H. J. Bensted

RUIZ CASTAÑEDA, M. Laboratory Diagnosis of Brucellosis in Man. *Bull. World Health Organization*. Geneva. 1961, v. 24, No. 1, 73-84. [17 refs.]

In a disease of such protean manifestations as brucellosis it is easy to become impressed by its probable presence when diagnosis rests on slender grounds. The author gives a sober presentation of laboratory methods which if followed would enable an unequivocal diagnosis to be made in many cases. He describes in great detail the methods to be employed in collecting samples for examination and the recipes for the preparation of suitable media, if satisfactory commercial products are not locally available. In appendices he gives details of other tests which he considers are appropriate only for more specialized laboratories. Care is required in dealing with live brucellae as infection is easily acquired accidentally in the laboratory.

No method is so satisfactory as the isolation of the organism but this is accomplished progressively less frequently the more chronic the infections. The author has devised a double-phase medium, liquid below and solid on the side of the container above. By tilting the container every few days, a series of attempted subcultures are performed and only when a growth is seen on the solid medium need the container be opened. A culture should be carried out under normal atmospheric conditions and also, to facilitate the growth of the classical strain of *Brucella abortus*, in a mixture of air with 10% CO₂. Details of how the carbon dioxide can be added to the air in the container are given.

Inoculation into guineapigs is a valuable procedure for the isolation of brucellae from highly contaminated material, penicillin being added.

Standardized antigens should be used for serodiagnostic tests when the results can be recorded in International Units (IU), a titre of over 100 IU being required to support the diagnosis, although it is noted that some cases have yielded positive cultures but failed to yield this titre.

Details of two simple rapid tests, the "Spot test" and the "Surface-fixation test" are given. These are useful as screening tests and if positive might justify the commencement of antibiotic treatment. The intradermal test is regarded of value chiefly as a public health measure in determining the epidemiology of the disease.

[This article has the approval of a number of named authorities of international repute and requires no other approbation.] Frederick J. Wright

MARTIN, W. J., NICHOLS, D. R. & BEAHR, O. H. Chronic Localized Brucellosis. With recurrent Constitutional Manifestations. *Arch. Intern. Med.* 1961, Jan., v. 107, No. 1, 75-80. [10 refs.]

The authors use the term localized brucellosis if a specific tissue such as the lung, spleen or kidney has

yielded a *Brucella* on culture after evidence of bacteraemia had been lacking. In such cases it is stated that agglutinins may be absent or detectable only in a low titre. The patient may suffer from few symptoms but rarely he exhibits recurrent fever and other signs. The case history is given of a meat packer, aged 35 years, who had suffered from a bout of fever about every 2 years during the years 1948-57 but in the 9th year of his illness suffered from 3 attacks of fever and in the 10th year from 8 attacks. During the last attack he had felt pain in the region of the spleen. It was ascertained that in 1947 the brucellar agglutination titre had been 1:2,560 and since that time had been at a level of 1:320. Repeated cultures of the blood and urine were negative. The spleen was just palpable and radiography showed calcification in it. The spleen was removed and was found to contain multiple caseous granulomata up to 5 mm. in diameter. *Brucella melitensis* was cultured from these lesions but not from the liver. Streptomycin and tetracycline were administered for 4 weeks after the operation. The patient has remained well since.

The authors also tabulate the data in 4 other cases of chronic localized brucellosis, all due to *Brucella suis*, which they have observed and which have been previously published [see, for example, this *Bulletin*, 1952, v. 27, 655; 1957, v. 32, 662; 1959, v. 34, 1111]. They note that during the years 1940 to 1958, of 224 cases of brucellosis seen at the Mayo Clinic 36 yielded *Brucella* only from localized tissues, 31 of these were asymptomatic or had had symptoms for less than 1 year, the other 5 are those referred to above and, in these, symptoms recurred over periods ranging from 10 to 17 years. In 4 of the 5 the spleen was enlarged and yielded *Brucella* on culture. In one case *Brucella* was cultured also from the liver but in one case only from an enlarged inguinal lymphatic gland connected with a chronic sinus.

Frederick J. Wright

VERSHILOVA, P. A. **The Use of Live Vaccine for Vaccination of Human Beings against Brucellosis in the USSR.** *Bull. World Health Organization*. Geneva. 1961, v. 24, No. 1, 85-9. [17 refs.]

Sheep and goats infected with *Brucella melitensis* are the source of infection of 85% to 95% of all overt human brucellosis in farming areas of the Soviet Union. The infection in sheep and goats has remained at a high level but the incidence of human brucellosis has fallen during the period 1952-58 by 59.5%. This reduction in frequency is attributed largely to the use of a live vaccine given subcutaneously and in later experiments intracutaneously. A variant of the strain *Br. abortus* 19 (Buck Cotton), named 19-BA by the author, has been used and a dried live vaccine prepared.

In a dose of 300-600 million brucellae this vaccine proved to be immunogenic and harmless. Local and general reactions were not severe except in the case of those who had suffered from brucellosis in the past or had prolonged contact with brucellae. Of those whom the vaccine failed to protect, 33% acquired the infection within 2 months of vaccination and 35% after 9 months. Those who acquired the infection between 2 months and 1 year after vaccination suffered only from a mild modified disease. It is therefore recommended

that re-vaccination should take place a year after the primary vaccination but, to avoid severe reactions, it is proposed that the re-vaccination should be intradermal.

Research into the effectiveness of a new strain *Br. abortus* 104-M is also being carried out.

[Protection by live vaccine of personnel at risk appears to be fully justified by this report.]

Frederick J. Wright

KNOTHE, H. & HAVEMEISTER, G. Ein Beitrag zur Serologie der Tularämie (Hämagglutination, Agglutination, Paraagglutination und Agglutininabsorption). [Contribution to the Serology of Tularaemia] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 1, 80-102, 4 figs. [26 refs.]

The authors have applied to the diagnosis of tularaemia the well-established technique of sensitizing red blood corpuscles with bacterial antigen and observing the agglutination of such cells by the sera of patients suspected to be suffering from the disease. In all, 150 samples of serum taken at various stages of the disease have been examined. The lipopolysaccharide antigen used for sensitizing the corpuscles was prepared by methods previously described by the authors (*Ztschr. f. Hyg. u. Infektionskr.*, 1960, v. 146, 527).

When this method is compared with the direct agglutination of *Brucella tularensis* by sera the following advantages are observed: (1) recognition of antibody earlier in the course of illness—5th day; (2) absence of prozone phenomena; (3) recognition of cases showing only slight immune response.

Cross-agglutination with the sera of *Brucella*-infected patients is a difficulty but not an insuperable one as the homologous agglutination titre is ultimately higher and the technique of absorption of agglutinins can be applied as in direct reactions between bacteria and antisera.

J. W. McLeod

PATEL, J. C., DHIRAWANI, M. K., MEHTA, B. C. & VERDHACHARI, N. S. **Tetanus following Vaccination against Small-Pox.** *Indian J. Pediatrics*. 1960, July, v. 27, No. 150, 251-3.

Of 2,007 cases of tetanus at the King Edward Memorial Hospital, Bombay, between November 1954 and October 1958, 20 were shown to follow smallpox vaccination, 18 after primary vaccination. The 2 children revaccinated were aged 5 and 6 years, the 18 other children were between 3 and 15 months old. The authors were satisfied that the vaccination sore was the portal of entry though no mention is made of bacteriological findings. The mortality in the 20 cases was 35%, compared with 43.7% in the total 2,007 cases.

A. B. Christie

WILLIAMS, H. W. & CHAFEE, F. H. **Demyelinating Encephalomyelitis in a Case of Tetanus treated with Antitoxin.** *New England J. of Med.* 1961, Mar. 9, v. 264, No. 10, 489-91, 4 figs. [10 refs.]

A 13-year-old boy suffering from tetanus was treated with large doses of tetanus antitoxin. The tetanus

appeared to respond to treatment and convulsions were controlled. On the 8th day of the illness he developed urticaria and oedema of the eyelids and on the 11th day he sank into coma and died. At autopsy a myriad of pin-point lesions were found in the white matter of the brain: the histological appearance was one of perivascular demyelination similar to that found in experimental allergic encephalitis. The lesions were regarded as probably an allergic response to tetanus antitoxin: reference is made to similar reports in the literature [see, for example, this *Bulletin*, 1954, v. 29, 912].

A. B. Christie

GROND, J. T. H. Tetanus-preventie bij rampen. [Prevention of Tetanus in Times of Disaster] *Nederl. Tijdschr. v. Geneesk.* 1961, Jan. 21, v. 105, No. 3, 117-21. [14 refs.] English summary.

The problem of tetanus during periods of national disasters (*i.e.*, war) is discussed. It is pointed out that surgical procedures play only a small role in the prevention of tetanus, 40% of cases being due to wounds so minor that medical aid is not sought. Incidence and mortality are discussed with reference to German and Italian figures, as are examples of the incidence in war casualties.

A discussion of passive immunization illustrates its limitations, especially regarding serum sickness and anaphylaxis and also the diminished effect on subsequent administration. The merits of active immunization are outlined and especially urged in war-time. A scheme of immunization of adults up to 45 years of age (83% of cases are under that age) is suggested and the family doctor is considered the most suitable person to carry out this project. It is also urged that combined active and passive immunization of patients should be routine.

Tetanus as a possibility in biological warfare receives attention and a high level of immunity is considered the only practical form of defence. Kurt Schwarz

HOOGENDOORN, D. Beschouwingen over de wenselijkheid, ook oudere kinderen en volwassenen tegen tetanus in te enten. [Should Older Children and Adults be immunized against Tetanus?] *Nederl. Tijdschr. v. Geneesk.* 1961, Jan. 21, v. 105, No. 3, 121-4, 2 figs. English summary.

The advisability of an extensive programme of active immunization against tetanus in adults (up to 45 years of age) is discussed. Incidence figures, mortality rates with age and sex distribution of tetanus are presented.

It is calculated that 1 tetanus death could be prevented by inoculating 234,500 persons—assuming 90% effectiveness of the immunization—but there are administrative difficulties in carrying out the programme, especially if voluntary cooperation of the public is required; possible complications of inoculations (infection, errors, serum hepatitis) should also be taken into account, and the author concludes that in peace-time a programme of this type is not warranted. Kurt Schwarz

LAURENCE, D. R. & WEBSTER, R. A. Activity of the Triethyl Analogue of Choline in suppressing Experimental Tetanus. *Lancet.* 1961, Mar. 4, 481-2, 1 fig.

The triethyl analogue of choline, N-tri-ethylaminoethanol, inhibits the synthesis of acetyl choline at neuromuscular endings. It appears to have a greater blocking effect on rapidly firing motor nerves than on those conducting fewer impulses and might therefore have a selective effect in controlling muscles in tetanic spasm while sparing the muscles of respiration and other normally acting muscles. In experiments in rabbits, with induced local tetanus, this appeared to be the case: tetanus was reduced by 68% over 1½ hours with a dose of 50 mgm. per kgm. body weight, and by 39% with 25 mgm. per kgm. A. B. Christie

MARSHALL, V. & SIMS, P. Gas Gangrene after the Infection of Adrenaline-in-Oil, with a Report of Three Cases. *Med. J. Australia.* 1960, Oct. 22, v. 2, No. 17, 653-6, 2 figs.

Case 1. In October 1940, a male aged 48 years was given an injection of 1 ml. of adrenaline-in-oil into the right deltoid muscle for an attack of asthma. 15 hours later the arm became painful and swollen; extensive cellulitis of the arm appeared and this was followed by dusky discolouration of the skin. The patient collapsed and died about 38 hours after the initial injection. Autopsy revealed *Clostridium welchii* necrosis of the muscles of the shoulder and pectoral region. Other ampoules of the same batch of adrenaline-in-oil were sterile. The syringe and needle were cultured [exactly when is not stated] and were found to be sterile; they had been kept in methylated spirit.

Case 2. In March 1959, a male aged 43 years was given an injection of adrenaline-in-oil into the right buttock for the treatment of urticaria. Some 12 hours later the buttock became painful and swollen and two days later a diagnosis of gas gangrene was made and confirmed at operation 9 days after the injection. *Cl. welchii* was isolated from thin, blood-stained fluid aspirated from the site at the time when the first symptoms appeared. With appropriate surgery and penicillin treatment the patient survived and left hospital after nearly 2 months of illness. [No details are given about the syringe and needle.]

Case 3. In May 1959 a man aged 52 years was similarly treated with an injection of adrenaline-in-oil into the left buttock for the relief of asthma. Simultaneously with the injection, a course of chloramphenicol was begun. Within 12 hours he showed the first signs of gas gangrene, from which he died in another 17 hours despite vigorous surgical and medical treatment on orthodox lines. The syringe used for the injection had been kept in a 1 in 1,000 solution of "Zephiran". This solution and other relevant materials in the case were all cultured for *Cl. welchii* with negative results.

These events are discussed with emphasis on the ability of adrenaline to enhance anaerobic infections by reason of its vaso-constricting effect and consequent reduction of oxygen tension. [See also: COOPER, *Lancet*, 1946, v. 1, 459 and TONGE, this *Bulletin*, 1958, v. 33, 603.] J. W. Howie

BISHOP, Ruth F. & MARSHALL, V. **The Enhancement of *Clostridium welchii* Infection by Adrenaline-Oil.** *Med. J. Australia.* 1960, Oct. 22, v. 2, No. 17, 656-7.

As a sequel to the work described in the preceding abstract, experiments on guineapigs were devised to assess whether the oil still further enhanced the significant enhancing effect of adrenaline on *Cl. welchii* infection. Infection was made by injecting from 5×10^3 to 5×10^8 washed *Cl. welchii* into the hind leg along with: (a) Ringer's solution; (b) arachis oil; (c) adrenaline in oil; (d) adrenaline in aqueous solution. Infection was enhanced one-thousandfold by adrenaline, but there was no difference between the oily and the aqueous solutions. The oil alone did not enhance the experimental infection.

J. W. Howie

FÜZI, M. & KISZEL, J. **Leptospirosis Studies in the Tápíó Region.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 383-90. [16 refs.]

Although human leptospirosis had been demonstrated in every region of Hungary, until 1954 the incidence in the central region (between the rivers Danube and Tisza) had appeared to be low. In the summer of 1954 an outbreak occurred in this region and 22 persons were affected with a non-icteric, mainly mild, illness.

Agglutination-lysis tests were carried out on paired sera from 10 of these patients: all the first samples (obtained on day 5-6 of illness) were negative; but the "convalescent" samples were positive (at titres of 1 in 200 to 1 in 1,800) against *Leptospira pomona* (4), *L. grippityphosa* (4), or *L. hyos* (2). The following additional serotypes were used as antigen in the tests: *icterohaemorrhagiae*, *ballum*, *australis A*, *australis B*, *hebdomadis* and *sejroe*.

The outbreak involved 3 groups in neighbouring foci in and around the agricultural settlement of Tápíószentmárton in the northern part of central Hungary. One group was of 5 children who often bathed in shallows of the river Tapio as it entered the village from the pastures; serological tests were not performed. The second group was of 10 labourers on the near-by farm, most of whom worked in the vineyards but who often bathed in the river near an area where numerous pigs, cattle and sheep were pastured: serological tests (*pomona*, 4; *hyos*, 1) tended to incriminate domestic animals as the source of infection. The third group was of 7 farm labourers who worked in sodden meadows about 8 km. from the village and far from the river (in which none had bathed): serological tests (*grippityphosa*, 4) suggested that field rodents, known to be carriers of *L. grippityphosa* in Hungary, were responsible.

A serological survey of domestic animals was carried out; titres of 1 in 100 or higher were regarded as significant and the seropositivity rates were: pigs, 84% (42/50); cattle, 32.5% (13/40); sheep, 9.5% (4/42). Neither illness suggestive of leptospirosis, nor frequent abortions, had been observed on this farm during the preceding 3 years. The predominant serotypes (alone or in combination) were as follows: pigs—*hyos* (26), *pomona* (21) and *sejroe* (7); cattle—*pomona* (10), *sejroe* (4), *grippityphosa* (1); sheep—*icterohaemorrhagiae* (4).

The findings serve to emphasize several points. (1) Leptospirosis in animals and sporadic cases in human beings are often difficult to recognize except with laboratory aids. (2) Different serotypes, and different modes of transmission, may be concerned in relatively localized outbreaks. (3) Outbreaks of leptospirosis in human beings need particularly favourable conditions: large numbers of sources of infection, humidity and numbers of susceptible persons at the contaminated site. (4) Human leptospires commonly occur sporadically.

L. H. Turner

CHERNOUSOVA, A. V., KORNILOVA, A. L. & SUKTA-MOVA, G. G. **Ictero-Haemorrhagic Leptospirosis in a Remote District of the Novosibirsk Oblast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 6, 1147-9. [Translated from Russian.]

KRASIL'NIKOV, A. P. & GRITSKEVICH, A. V. **Anthropurgic Foci of Leptospirosis in Belorussia. 1. Infection of Domestic Mice with *Leptospira hebdomadis*.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 6, 1150-55. [27 refs.]

HAVLÍK, O., POKORNÝ, J. & ZÁSTĚRA, M. **Method of Experimental Research in a Focus of *Leptospira*.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 494-503, 5 figs. [10 refs.]

Hitherto, studies of infection rates in reservoir hosts of leptospirosis have been based on collections obtained during a single expedition or on several collections, obtained at intervals, from one trapping area [or on animals obtained over a considerable period].

The authors avoided the inadequacies of earlier "static" methods of investigation by using a "mark-release-recapture" technique which is more "dynamic". Mice [see below] were captured alive and examined (weight, sex); and blood was obtained for serological testing. Animals were marked by amputation of a toe or ear (a system which allows a total of 800 combinations) so that individuals could be recognized; and each animal was then released, as soon as possible, at the site of its capture.

An earlier investigation had shown that, in an area of north-west Bohemia, *Leptospira grippityphosa* was the only serotype present (134 strains isolated) and that the field mouse (*Microtus arvalis*) was the main reservoir host. In this area, two localities separated by about 1 km. were chosen for the present study: one was cultivated fields, the other was unkept meadow at the forest fringe. During 1958 and 1959, 8 expeditions (4 each year) were made [at irregular intervals] to these localities. Each expedition lasted 12 days and a large number of traps was used. The authors consider that they caught and examined practically all the field mice in the localities on each occasion. A total of 1,469 field mice were examined; 21.5% were recaptured at some time. Infection rates were based on agglutination-lysis tests and

titres of 1 in 100 or higher were regarded as significant for this purpose.

Proper assessment of the results of an investigation such as this requires knowledge of the ecology of the reservoir hosts, of environmental factors (rainfall, etc.), and of the method of transmission of the infection.

The findings, in summary, were as follows:

(1) A significant rise in antibodies occurred in 14.9% of recaptured mice: this figure compares with the overall seropositivity rate (15.0%) in all the animals.

(2) The seropositivity rate varied with the year, season, locality, sex (males, 18%; females, 10.2%), and weight (higher in heavier animals).

(3) In 1959, seropositivity rates were higher for both localities than in 1958; moreover, the titres tended to be higher (median for 1958, 1 in 300; 1959, 1 in 10,000).

[Those who may be interested in carrying out similar investigations are advised to study the original paper.]

L. H. Turner

PIKE, R. M. & SCHULZE, Mary L. **Incidence of Leptospiral Agglutinins in Patients. A Ten Year Experience.** *J. Lab. & Clin. Med.* 1961, Feb., v. 57, No. 2, 223-9. [15 refs.]

Human leptospirosis is being recognized with increasing frequency in the United States. The present report summarizes the findings in agglutination tests carried out on sera from 521 hospital patients between 1950 to 1959 inclusive. In some of these patients leptospirosis was suspected, in others (many jaundiced) it was to be eliminated as a possible aetiological factor. Living suspensions of the following 8 serotypes of *Leptospira* were used in the tests: *icterohaemorrhagiae*, *canicola*, *pomona*, *grippityphosa*, *bataviae*, *hebdomadis*, *autumnalis A* and *autumnalis AB*. Sera were first examined at a final dilution of 1/100 with each of the 8 serotypes; those which reacted were then titrated against serial 2-fold dilutions of the serum. Altogether 31 patients (6%) were found to give positive reactions (1/200 or higher) with one or more serotypes: the incidence was higher (11.8%) at one hospital where a higher proportion of patients came from rural areas, than in the other (3.8%) where the patients comprised a predominantly urban group. At the end of a period of dry years the overall incidence was low (2%) in contrast to that during an unusually wet year (14%).

The predominant serotypes were found to be *canicola* (13), *pomona* (12), and *grippityphosa* (6). Heterologous reactions were common—with *icterohaemorrhagiae* in the "canicola" group (10 out of 13), and with *autumnalis* in the "pomona" group. Positive reactions were obtained on day 4 of illness in 2 cases; but 3 others were negative at day 5, one at day 7 and one at day 13; and a significant titre was not demonstrated in one patient until 3 weeks.

The serum of one patient, from whom a leptospire was isolated, reacted with *L. pomona* and 5 other serotypes. Serum of a rabbit immunized with the isolated strain was compared with the patient's serum in agglutination tests with the 8 serotypes and the isolate. The qualitative results were essentially similar but the titres obtained with the rabbit serum did not tend to support the antigenic relationships which were suggested by the

findings in the patient's serum. Results also seemed to indicate that heterologous reactivity of the rabbit serum diminished with time: serum obtained 21 days after the last immunizing dose was compared with serum obtained on the 7th day. (The rabbit was immunized with 5 doses of 1 ml. of live culture, one dose each day.)

L. H. Turner

BABUDIERI, B. **Laboratory Diagnosis of Leptospirosis.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 1, 45-58, 1 fig. [30 refs.]

[This is a lucid and comprehensive account of the subject which deserves to be read by clinicians as well as laboratory workers since only a few of the more important points can be mentioned in an abstract.]

(1) *Direct observation and staining*: dark ground microscopy and silver impregnation methods, as for other spirochaetes, are used.

(2) *Culture requirements*: leptospire grow in liquid media, and in [not on] semi-solid and solid modifications of these, of which the basic constituents are salts buffered to pH 7.2, rabbit serum (5-10%) and peptone. Cultures are incubated in the dark at 28-30°C., but growth is slow (7-30 days).

(3) *Maintenance of cultures* for diagnostic purposes is primarily a duty of the reference laboratories, but diagnostic laboratories should maintain at least one strain of each serotype which naturally occurs in their country.

(4) *Examination of specimens*: direct search for leptospire is seldom fruitful in blood, but is worth attempting on the centrifuged deposit of freshly voided, alkalized urine. Leptospire can be isolated by culture or by inoculation (intraperitoneal) of young hamsters or guinea-pigs. Blood culture should be attempted during the first week of illness and urine culture after the first week. Laboratory animals may show little if any sign of infection; cultures from heart blood should therefore be made after 6-7 days or if the animal becomes febrile. Kidney cultures can be made from surviving animals at 20-30 days and serological examination for antibodies should also be undertaken.

Serological diagnosis should be based on a significant rise of antibody levels, not on absolute values obtained on single specimens. Antibodies are seldom demonstrable during the first 7 days of illness, usually reach their peak by 15-20 days and thereafter persist for a variable period depending on the infecting strain and the individual patient. Antibiotic treatment may influence the antibody response which may be delayed (for about 3 weeks), depressed or even inhibited altogether. The specificity of the available serological reactions varies in the following (descending) order: agglutination, complement fixation, haemolysis. Cross-reactions commonly occur with other serotypes and specific diagnosis of the infecting serotype by means of serology can be difficult. Strains isolated by culture are identified by means of agglutination-absorption studies.

This paper includes a list of pathogenic *Leptospira* subdivided by serogroups (18), serotypes and subserotypes (altogether 60) which has since been enlarged: this illustrates the increasing complexity of the genus as more study is made of it.

L. H. Turner

COHN, A. P. & HOWARD, A. A. **Common Characteristics of Leptospirosis: a Report on 11 Cases.** *Ann. Intern. Med.* 1961, Jan., v. 54, No. 1, 57-65. [12 refs.]

Clinical and laboratory findings in 11 U.S. Marines involved in an outbreak of leptospirosis on Okinawa are presented: they support several recent observations that leptospirosis commonly presents as a mild illness. The 11 men had all swum in a natural, apparently stagnant, pond 9-14 days before the onset of symptoms.

The incidence of initial symptoms and signs was as follows: fever, chills, headache, anorexia—11; myalgia—10; conjunctivitis, retro-orbital pain—7; nausea and vomiting, diarrhoea—6; herpes simplex labialis, nuchal rigidity—5; abdominal pain—4; meningitis—3; pneumonitis—1. None of the patients had enlargement of spleen or liver, and none was jaundiced.

The main laboratory findings included: leucocytosis—9; raised serum glutamic-oxalacetic transaminase values (over 40 units)—9; abnormal urinary sediment—8; albuminuria—8; cerebrospinal fluid pleocytosis (more than 10 cells per cmm.)—3; raised serum bilirubin—1. Azo-taemia was not demonstrated in any of the 11 patients.

Liver biopsy was performed on 2 patients who had one or more abnormal liver function tests: both specimens consisted of normal liver. 4 serotypes were used for agglutination tests on acute and convalescent phase samples of serum of 10 of the patients: *Leptospira autumnalis* A, *L. hebdomadis*, *L. semarang* and *L. australis* (Ballico). The titres obtained were diagnostic of leptospirosis but, as so often happens, the findings did not indicate the infecting serotype: cross-reactions to about the same titre were very common. Isolation of leptospires was impracticable.

Treatment with tetracycline (1.0 gm. initially, followed by 0.5 gm. every 6 hours) was started on the 4th to 8th day of illness in 10 cases; chloramphenicol (in the same dosage) was started 24 hours after the onset of symptoms in the other. It was considered that the chemotherapy had little effect on the illness of these patients (but it had been started somewhat late).

L. H. Turner

CLARK, L. G., KRESSE, J. I., MARSHAK, R. R. & HOL-LISTER, C. J. ***Leptospira pomona* Infection in an Eastern Red Fox (*Vulpes fulva fulva*).** [Correspondence.] *Nature*. 1960, Dec. 17, v. 188, 1040-41.

Bovine leptospirosis is known to occur in Pennsylvania. At present the relationship between bovine and sylvan leptospirosis is being investigated in the south-eastern parts of the state: infected cattle herds are identified and their premises are then intensively trapped for wildlife. Trapped animals are examined for infection by serological and cultural techniques.

Isolations of leptospires have so far been made from the woodchuck, opossum, skunk, racoon and *Rattus norvegicus*.

The authors now report the isolation (believed to be the first) of *Leptospira pomona* from an eastern red fox (*Vulpes fulva fulva*) trapped on a farm where this serotype had been isolated from the cattle and from surface

water. Growth of this isolate was detected 34 days after inoculation of media with kidney material. Serological titres (microscopic agglutination test with living antigen suspensions) were obtained with *L. pomona* (1 in 100) and *L. autumnalis* (1 in 1,600) but not with the following serotypes: *bataviae*, *ballum*, *canicola*, *icterohaemorrhagiae alexi*, *grippotyphosa*, *australis* A, *sejroe* and *hyos*.

L. H. Turner

PANDE, P. G., SEKARIAH, P. C. & SHUKLA, R. R. **Examination of *Leptospira pomona* by Gel Diffusion.** [Correspondence.] *Nature*. 1961, Feb. 11, v. 189, 511-12.

4 strains of *Leptospira pomona* were subjected to antigenic analysis by means of the gel diffusion method with the technique of MANSI [*J. Comp. Path. & Therap.*, 1957, v. 67, 297; this *Bulletin*, 1959, v. 34, 266] and hyper-immune rabbit sera. In homologous test systems 2 of the strains gave 2 reaction zones while the others produced only 1. In reciprocal systems one common major line was noted.

When antigenic fractions prepared according to the methods of SCHNEIDER [this *Bulletin*, 1954, v. 29, 1190] were tested against the homologous whole-cell antisera, no line was detected with fractions 3 and 4: this might indicate that these antigens are located deep in the cell. Fraction 2 appeared to determine differences in serological reactivity while the other 3 were common to all the strains.

Saline extracts of kidney lesions gave strong reactions with immune rabbit serum. The test was also satisfactory when used with infected tissues preserved in 5% formalin or 50% glycerin; this method will therefore be used to investigate material from suspected cases of leptospirosis in domestic animals in India.

The test also was successfully applied to detect antibodies in sera in suspected leptospirosis. An estimation of the sensitivity and reliability of this method is in progress.

L. H. Turner

DELAHOUSSE, J., ROUSILHON, J. P., BOYER, G. & BORDES, F. P. **Utilité du traitement antibiotique précoce dans les leptospiroses. [Value of Early Antibiotic Treatment in Leptospirosis]** *Méd Trop. Marseilles*. 1961, Jan.-Feb., v. 21, No. 1, 38-44. [15 refs.]

To date there has been a lack of agreement regarding the value of antibiotics in the treatment of leptospirosis, which can be attributed to the relative scarcity of cases in temperate climates and to differences in dosage and the time at which treatment was instituted. A review of the literature indicates that antibiotic therapy is of considerable value provided that (i) the dosage is adequate, and (ii) treatment is commenced early in the course of the illness. Experimental evidence suggests that this concept is true whatever the causative serotype may be, but the efficacy of antibiotics differs as follows (in descending order)—penicillin, streptomycin, tetracycline, oxytetracycline, chlortetracycline.

The authors present data which, they claim, support the concept stated above. The data were derived from

cases among military personnel and prisoners who had operated in the jungles of South-East Asia ("Indo-China"). All the troops were cared for by the same unit and treatment was commenced on admission. The duration of illness at the time of admission depended on how quickly the patients had reached the hospital. Diagnosis was confirmed in due course by serological tests on the basis of which the incidence of infecting serotypes was—*Leptospira bataviae*, 25%; *L. australis*, 25%; *L. canicola*, 18%; *L. icterohaemorrhagiae*, 18%; *L. hebdomadis*, 12%; and *L. grippotyphosa*, 2%. (All these serotypes had been isolated previously in the same region.) Antibiotics were given to every patient, regardless of his clinical condition: either penicillin (injections every 3 hours; total dosage, 2-4 mega units per day), or chlor-tetracycline (2-3 gm. per day). The tabulated results (simplified) were as follows:

Onset of treatment	No. of patients	Clinical types (%)			Mean duration of hospitalization	Relapse/complications	Deaths
		Simple	Inter-mediate	Grave			
(day of disease)					(days)	(%)	(%)
1-3	58	89.5	6.9	3.5	9	6.8	0
4, 5	19	31.5	31.5	36.8	27	26.3	0
6-	27	22.2	7.5	70.3	40	22.2	22
Untreated controls (prisoners)	29	49	10	41	—	—	17.2

[It is unfortunate that no distinction is made between results in patients treated with penicillin and those given chlortetracycline.]

L. H. Turner

HOOD, M. **Listeriosis as an Infection of Pregnancy manifested in the Newborn.** *Pediatrics*. Springfield, Ill. 1961, Mar., v. 27, No. 3, 390-96. [32 refs.]

At the Charity Hospital, New Orleans, 29 cases of infection with *Listeria monocytogenes* were recognized in approximately 5 years. In 5 cases the patients were debilitated adults, 4 of whom died. 5 patients were pregnant women and in them the infection took the form of a febrile illness with malaise. In 2 of the 5 the illness was diagnosed and treated before delivery; the first woman was fully treated and subsequently gave birth to a normal child; the second woman was inadequately treated and her infant developed meningitis due to *Listeria monocytogenes* on the 8th day of life. 18 other infections in children were diagnosed, the ages ranging from birth to 6 years. The commonest manifestation in children was meningitis. There was no evidence from extensive bacteriological surveys that the infection was endemic in the area. The author feels that some control is possible if febrile illnesses in pregnant women are fully investigated and if infants born from women who

show signs of uterine sepsis are carefully watched during the neonatal period. The organism is sensitive to most antibiotics.

A. B. Christie

KING, Sylvia & BRONSKY, D. ***Vibrio fetus* isolated from a Patient with Localized Septic Arthritis. Recent Evidence suggests that this Infection is Less Rare than Figures indicate.** *J. Amer. Med. Ass.* 1961, Mar. 25, v. 175, No. 12, 1045-8, 1 fig. [11 refs.]

Vibrio fetus is an important cause of abortion in cattle and sheep. The mode of transfer of infection to man is unknown. The symptoms are usually those of a generalized systemic infection. In the present case, a man aged 74 developed septic arthritis of the knee following minor injury. He had not been ill recently. *Vibrio fetus* was grown from the fluid aspirated from the joint. The condition responded to oral treatment with 1 gm. of chloramphenicol daily.

A. B. Christie

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.*

UTTLEY, K. H. **Smallpox Mortality in the Negro Population of Antigua, West Indies; a Historical Note.** *West Indian Med. J.* 1960, Sept., v. 9, No. 3, 169-71.

Registration of deaths in Antigua was introduced in 1856, but before this smallpox must have been a severe scourge there because a number of ordinances were enacted in an effort to control it. One of these prevented any unvaccinated individual from obtaining judgment on any complaint of a civil nature in any court of law.

No deaths from smallpox on the island occurred between 1856 and 1860. During the next 5 years 267 persons died of the disease, whose main prevalence was in the winter and spring months—those with the lowest humidity.

Since 1865 no death from smallpox has occurred in Antigua, in spite of frequent outbreaks [? variola minor ? variola major] elsewhere in the Caribbean.

[Figures given relate to mortality only. No attempt is made to assess the incidence of the disease or the immunity of the population.]

J. Pickford Marsden

KEEVILL, A. J. **A Little-Known Complication of Smallpox in Tanganyika.** *East African Med. J.* 1960, Oct., v. 37, No. 10, 692.

In central Tanganyika there was an old custom of treating smallpox in young people by hyperextension and traction of both elbows (and sometimes of both

ankles) until they "cracked", so as to "bring out the rash". The result was often fracture-dislocation and consequent ankylosis. The custom, fortunately, is dying out.

Charles Wilcocks

KRAVITZ, H. A Simplified Technique for Vaccination against Smallpox. *Pediatrics*. Springfield, Ill. 1961, Feb., v. 27, No. 2, 219-26, 6 figs. (1 coloured). [18 refs.]

The new weapon consists of a plate about 1 cm. square made either of stainless steel or plastic, carrying 9 points either 0.15 cm. long with a total scarifying surface of 0.35 cm., or 0.21 cm. long with a scarifying surface of 0.29 cm. The weapon, mounted in a strip of adhesive bandage, was applied to the arm by applying pressure with the thumb; or, alternatively, by direct pressure from a unit mounted on the thumb of the vaccinator.

6 series of unvaccinated infants were treated in these ways. In some the vaccine was first applied to the skin; in others the vaccine material was dropped directly on to the points of the scarifier. A further series of children as controls were vaccinated by the more usual multiple pressure method.

The highest percentage of takes (100%) occurred in those cases (40) in which a plastic thumb unit with vaccine impregnated 0.21 cm. points on 0.29 cm. square base was used. [But, on the whole, the figures given are not statistically very significant.]

The new vaccinator is said to provide uniformly smaller and cosmetically superior scars.

[In vaccinating it has always been a case of *Chacun à son goût*. Results matter more than the method.]

J. Pickford Marsden

ZIMÁK, V., FOSENBAUEROVÁ, E. & PEYCHL, L. Post-vakcinační encefalitida. [Postvaccination Encephalitis] *Časopis Lékařů Českých*. Prague. 1961, Mar. 3, v. 100, No. 9, 264-8. [13 refs.]

The English summary appended to the paper is as follows:—

"In the present paper the authors discuss five cases with an acute affection of the CNS after vaccination against smallpox in autumn 1958. In three cases of first vaccinations the relationship between the vaccination and the disease seems to be beyond doubt. In one of these patients the course of the disease was very severe associated with prolonged unconsciousness. In the remaining two cases the affection of the CNS developed after the revaccination and might have been due to another cause. The authors summarize some data from the literature on the pathogenesis, clinical aspects and treatment of this disease and compare them with their own experience. In two severe cases they used, in addition to common comprehensive treatment, cortisone and conclude—despite the small number of cases thus treated—that corticoid treatment is a valuable contribution. Finally they emphasize the need to adhere to all precautions of vaccination and recommend to prolong the minimum interval between individual vaccinations."

READETT, M. D. & MCGIBBON, C. Neonatal Varicella. *Lancet*. 1961, Mar. 25, 644-5, 1 fig.

The authors—dermatologists—report two cases. In Case 1 the mother who had had an attack of chickenpox in her early childhood, showed no signs of illness during her pregnancy and puerperium. However, on the day before she was confined the baby's brother developed lesions of varicella, and on the 14th day of life the infant himself commenced what proved to be a mild attack of this disease.

In Case 2 the mother did not know whether she had ever had chickenpox, but on the day her baby was born her daughter developed this disease. Subsequently, on the 12th day of his life, the infant showed varicella lesions but had little constitutional disturbance.

Antibody-neutralization titres in the serum of both mothers were "normal for immune adults", so it appears that in these cases transference of passive immunity to the foetus was of a degree insufficient to confer complete protection.

J. Pickford Marsden

NAKAO, T. Primary Varicella Pneumonia. *Tohoku J. Exper. Med.* 1960, Oct. 25, v. 72, No. 3, 249-52, 2 figs.

Cases of primary varicella pneumonia so far reported have mostly been in adults. The present author records 3 cases in young children—and the first at any age reported from Japan.

In each case the rash and fever were well marked and accompanied by severe cough. Physical signs in the chest were slight; but definite X-ray changes were seen in each case. The white blood picture was not that of bacterial infection. All 3 patients recovered.

J. Pickford Marsden

ROTEM, C. E. Complications of Chicken-Pox. *Brit. Med. J.* 1961, Apr. 1, 944-7, 2 figs. [28 refs.]

Of the patients admitted to the Leicester Isolation Hospital in the period 1950-59 with varicella 6 showed radiological evidence of "disseminated pneumonia". In 2 of these cases the rash was profuse and in another haemorrhagic; while other patients were classified as cases of varicella gangrenosa (1), and meningo-encephalitis (1). All recovered.

5 patients showed encephalitic symptoms: the one patient who died also had some haemorrhagic features.

In another fatal case of chickenpox in a 1-year-old girl there were haemorrhagic lesions, and lesions were present in the upper air and alimentary passages.

In 3 patients the skin lesions became secondarily infected: in 2 the generalized rash was associated with a localized eruption of zoster. One of these last patients, aged 85, also suffered a pulmonary infarction; another, younger, man developed multiple pulmonary infarcts from thrombosis of spermatic veins, iliac veins, and inferior vena cava which was demonstrated *post mortem*. This condition was superimposed upon what at first appeared to be a mild attack of varicella.

J. Pickford Marsden

BERESTON, E. S. & ROBINSON, R. C. V. **Herpes Zoster and Varicella in Identical Twins.** *Arch. Dermat.* 1961, Mar., v. 83, No. 3, 503-4.

"After apparently simultaneous exposure of identical twins to varicella-herpes zoster virus, one child developed varicella, the other developed herpes zoster."

SCHMIDT, Nathalie J. & LENNETTE, E. H. **A Colorimetric Neutralization Test for Herpes Simplex, with Observations on Neutralizing and Complement-Fixing Antibody Levels in Human Sera.** *J. Immunology.* 1961, Feb., v. 86, No. 2, 137-45, 3 figs. [19 refs.]

A neutralization test for herpes simplex virus was performed by leaving dilutions of serum mixed with a constant amount of virus at 4°C. for 30 to 60 minutes, adding a standard number of chick embryo fibroblasts in suspension and incubating the cultures for 8 days. After that time, the colour of the phenol red in the medium indicated pH 7.3 or higher when virus multiplication had inhibited cell metabolism and pH 7.2 or lower when all the virus had been neutralized and cell metabolism was normal. (Previous experiment had shown that serum titres were the same when measured with 100 or 1,000 TCD50 so that minor variations in the dose of virus were unimportant.)

Neutralizing and complement-fixing antibody in serum from 30 recruits, who had suffered a mild respiratory illness and from whom herpes virus had been isolated, and in serum from 123 patients with disease of the central nervous system, were titrated against herpes virus. The same sort of results were obtained with both tests, and there was good linear correlation. Complement-fixing and neutralizing antibodies appeared at about the same time after infection, and increased at the same rate, although neutralization titres were higher on average. [This is in contrast to the situation with poliomyelitis, for instance, when neutralizing antibody appears long before complement-fixing antibody.]

The colour test is said to be easier to perform than neutralization tests in mice or eggs. Varying the amount of serum mixed with a constant amount of virus seems to make the test more sensitive than the reverse procedure. The authors conclude that the test is as useful as complement fixation for demonstrating antibody rises in the diagnosis of primary herpes infection.

Janice Taverne

MCDONALD, J. C. **Surveys of Acute Respiratory Disease in the Royal Air Force.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 440-46, 1 fig. [14 refs.]

Since 1954 acute respiratory disease has been studied in Royal Air Force personnel in the British Isles by the Public Health Laboratory Service in collaboration with the Royal Air Force Medical Service. Specimens (throat swabs and paired sera) have been examined, records and statistical data studied and planned surveys and vaccine field trials carried out.

The pattern of illness has been as follows: the number of respiratory infections began to rise in October, reaching a peak in December (mainly "feverish colds") and falling because of the Christmas break only to reach the highest incidence at the end of January and during February (mainly influenzal in type). The greatest incidence was in recruits during their 2nd to 9th weeks of service, their monthly hospital admission rate during the first 3 months of the year approaching 10%. After the recruit period, the incidence fell with advancing age. There was no important association with geographical location, size of station, place or type of work or degree of crowding.

The following considerations concerned those illnesses requiring hospital admission. Apart from 1954-55, influenza A1 virus caused epidemics in 1955-56, 1956-57 and the Asian strain thereafter; about 22% of RAF personnel in Great Britain were affected by the Asian strain during the autumn of 1957. Influenza B was epidemic in 1954-55 and again in 1958-59. Adenovirus infections mainly involved recruits; in 1955-56 type 7 was prevalent, in 1957-58 mainly type 4 and the remainder type 7 and in 1958-59 almost all the strains were type 3 but some 4 and 7 also. Serological evidence of infection with Sendai virus was detected in 5 of 257 paired sera in 1955-56; in retrospect this was probably para-influenza 1 since Sendai virus has never been isolated in Great Britain. In 1958-59, 8 strains of para-influenza 1 virus were isolated and serological evidence of infection with either para-influenza 1 or 3 viruses was demonstrated in another 28 illnesses. Coe virus was isolated from 4 recruits in 1957-58 and in 1958-59 48 strains were isolated from over 1,100 throat swabs, most of the isolations being made in November.

In vaccine field trials, the vaccinated and control groups were always selected by a random method and the results judged by "blind" observers. A reduction in influenza of at least 40% in 1952-53 and 35% in 1955-56 followed the administration of influenza A vaccines which contained virus strains similar to those causing illness. One injection of a polyvalent adenovirus vaccine given to recruits in 1959 reduced by about 70% illnesses that occurred more than one week after inoculation.

[This paper was presented at the International Epidemiological Symposium in Prague in February 1960 and much of its contents has been published previously.]

D. Taylor-Robinson

BELL, J. A., CRAIGHEAD, J. E., JAMES, R. G. & WONG, D. **Epidemiologic Observations on Two Outbreaks of Asian Influenza in a Children's Institution.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 84-9, 1 fig.

During the influenza pandemic of 1957-58 two outbreaks due to the Asian type (confirmed by laboratory tests) occurred in a children's residential institution in Washington, D.C. The first outbreak occurred between August 10 and September 15, was inexplicably slow in spread through the various houses, but finally attacked 69% of the 223 children then present. The attack rate declined with age from 100% at 3-5 years to 70% at 6-12 years to 47% at 13-17 years. This trend, in face of

a new strain, indicates either immunity from prior experience with heterologous influenza antigens or a more complete exposure among the younger children. The second outbreak occurred between January 31 and February 11, 1958, attacked all the houses almost simultaneously but was of short duration. In total, 28% of the 259 children present were attacked. The noticeable difference between the summer and winter outbreaks in rate of spread may conceivably be due to unidentified seasonal influences for the summer period would appear to have offered more opportunities for contact spread among a more susceptible population.

Of 152 children not in residence during the first outbreak 39% were attacked in the second outbreak; of the 107 children who were in residence during the first outbreak only 11% were attacked in the second outbreak. A substantial immunity had therefore persisted for at least 5 months. On the other hand 5 of the 65 (8%) who had clinical influenza in the first outbreak were also attacked in the second, so that (if one is prepared to accept the clinical diagnoses as without error) the immunity conferred was not 100%. Of 42 children who had no clinical attack in the first outbreak 17% were attacked in the second, a figure substantially below the 39% in the children who were not there during the first outbreak. In other words some would appear to have developed immunity without passing through a recognized illness.

A. Bradford Hill

GREENE, C. C., Jr. & BEAVER, G. T. **A Study of Mass Influenza Inoculation in a Large Industry.** *J. Occup. Med.* Chicago. 1960, Aug., v. 2, No. 8, 363-70, 2 charts.

In 1957 inoculations "designed to reduce only the incidence and severity of Asian Strain influenza" were offered free by the Pacific Telephone and Telegraph Company of California to their 93,288 employees; 56,818 (61%) accepted and in August and September each was given a subcutaneous injection of 1 ml. monovalent Asian Strain vaccine containing 200 CCA (chicken cell agglutination titre) units. The 400 CCA units per ml. vaccine now used was not then available. In April 1958 a questionnaire was sent to the 88,079 employees then on the pay roll; 76,136 (86.4%) completed questionnaires and of these 49,307 (64.8%) stated that they had been inoculated. The purpose of the questionnaire was to estimate the efficacy of the vaccine and to determine the employees' attitude to the immunization programme. Although the questions were answered by the employees themselves, no names were recorded on the questionnaires and no distinction was made between any illnesses which the employees would normally have described as "influenza".

The authors stress that their data are not such as would satisfy the requirements of a properly designed clinical trial because the inoculated and non-inoculated groups were inevitably self-selected, the influenza attacks diagnosed by the patients themselves, their statements were not verified and there was a 7-month time lag between inoculation and assessment. They hope, however, that the data will be of use to industry and medicine because of the large number of subjects involved and because in

their opinion "it would seem reasonable to assume that approximately the same degree of bias and errors in reporting would exist in each group". [The use made of the large amount of information given in this report therefore calls for a high degree of critical appreciation by the reader and the tabulated information will help in this, although it is impossible to assess the true effect of factors such as self-selection and "self-diagnosis" on the comparisons made between the inoculated group and the remainder.]

The facts obtained from the analysis of replies were that 21.9% of the inoculated said they had influenza compared with 29.6% of the non-inoculated. For men these proportions were 20.6 and 25.6% respectively and for women they were 23.1% and 32.4%. The differences were largely due to age-groups under 40. Thus in the 4 age-groups: under 21, 21-40, 41-60 and 60 and over, the proportion who said they had influenza among inoculated (with non-inoculated shown in brackets) were for men 18.9 (31.6)%, 20.9 (27.3)%, 20.2 (20.8)% and 18.4 (15.8)%, and for women 24.5 (40.8)%, 23.5 (33.5)%, 21.0 (23.0)% and 22.6 (20.5)%. The average number of days lost from work amounted to 1.95 and 2.88 among inoculated men and women who reported that they had had influenza compared with 2.54 and 3.11 respectively among non-inoculated. These averages increased with age among inoculated men from 1.47 at ages under 21 to 2.55 at ages over 60 and from 2.32 among non-inoculated men under 21 to 3.31 at ages over 60. In women the corresponding increases were 2.60 to 4.10 in the inoculated and from 2.81 to 4.45 in the non-inoculated. At all ages and sexes the average number of days lost per person reporting influenza was greater among the non-inoculated than amongst the inoculated. Various other aspects of the reported sickness experience are given in a series of tables, including the distribution of the subjects who reported attacks by number of attacks, duration of the severest attack and number of days lost from work. 73.9% of employees who were inoculated said that they felt that it did them some good and this included about 75% of the 13,123 inoculated employees who experienced one or more reaction symptoms. The general opinion of most of the employees was that such immunization programmes were beneficial. On the assumption that, had they not been inoculated, the inoculated employees would have had the same amount of absence as the remainder, the cost of the immunization programme was more than balanced by the saving due to the reduction of absenteeism.

[It is clear from the introduction that the authors have taken great trouble to emphasize the difficulties of assessing the true value of the inoculation procedure. Their warning is not repeated in "Conclusions" and it is to be hoped that casual readers will not consider these conclusions, which also serve as a summary, without reading the report in detail.] E. A. Cheeseman

WILT, J. C., HILDES, J. A., PARKER, W. L. & DELAAT, A. **Sendai Virus Antibodies in the Arctic.** *Canadian Med. Ass. J.* 1961, Feb. 11, v. 84, No. 6, 319-21, 2 figs. [19 refs.]

As part of a study on the incidence of virus antibodies in the Arctic [this *Bulletin*, 1958, v. 33, 929], sera were

collected from healthy inhabitants of 5 Eskimo communities, 1 Arctic Indian community and also from Eskimos without respiratory disease in 2 sanatoria. 2 communities had an incidence of complement-fixing (CF) antibodies to Sendai virus of 76% and 43% respectively (titres of 1 in 4 or more) but no CF antibodies to mumps virus. In communities in which CF antibodies were present to both mumps and Sendai antigens there was no correlation between the concentration of Sendai antibodies and mumps antibodies. This further suggested the independent occurrence of the 2 types of antibody.

Paired sera from 14 Winnipeg children with mumps showed significant increases in CF antibody titres to both viruses in 5 instances. This suggested that the mumps virus produced antibodies which reacted with the Sendai virus, as proposed by others [an extensive study was carried out by GARDNER, this *Bulletin*, 1961, v. 36, 91]. The reason for the discrepancy between this result and the results for the Arctic communities is not clear.

D. Taylor-Robinson

DUNCAN, I. B. R. & HUTCHISON, J. G. P. **Type-3 Adenovirus Infection with Gastrointestinal Symptoms.** *Lancet*. 1961, Mar. 11, 530-32, 1 fig.

An illness characterized mainly by diarrhoea, vomiting or abdominal discomfort but, in a few patients, by pharyngoconjunctival symptoms was investigated virologically in 2 families. Adenovirus type 3 was isolated in 18 of 34 specimens—in all of 4 conjunctival swabs, 1 of 3 throat washings, and in 13 of 27 stool specimens. No other viral or bacterial pathogens were isolated. A significant rise of adenovirus antibodies was found in the serum of one of the adults affected. There was thus strong evidence that adenovirus type 3 caused the illness. One of the infected families visited relatives while two members still had symptoms—1 had diarrhoea and 1 conjunctivitis; 4 days later 3 of the relative's children became ill—1 with conjunctivitis, 1 with vomiting and 1 with listlessness who also refused to eat.

A. B. Christie

CHANOCK, R. M., MUFSON, M. A., BLOOM, H. H., JAMES, W. D., FOX, H. H. & KINGSTON, J. R. **Eaton Agent Pneumonia.** *J. Amer. Med. Ass.* 1961, Jan. 21, v. 175, No. 3, 213-20. [17 refs.]

The authors made a systematic study of the role of this infectious agent [see also this *Bulletin*, 1960, v. 35, 676, 790, 1013] in young men under training at the Marine Corps Recruit Depot, Parris Island, South Carolina, between May and October 1959 when the average strength was 5,302 men. Sera were collected and tested for specific antibody by the fluorescent antibody method. Throat swabs were collected and tested by inoculation into monkey kidney cultures followed by sub-inoculation into 13-day eggs. Infected eggs were detected by staining lung sections with fluorescent antibody.

There was little evidence of adenovirus or influenza virus infection. Eaton agent was recovered from 14 of 17 cases of primary atypical pneumonia. Antibody rises

against Eaton agent occurred in 68% of 238 cases of this disease; of 137 recruits who subsequently developed the disease only 1.5% had detectable antibody when they began training whereas 17% of 165 recruits who did not develop pneumonia had antibody. Paired sera from 79 cases of pneumonia were compared with 110 matched controls from the same platoon or company. 59 patients showed an antibody rise and only 5 controls. These data indicate that the Eaton agent caused the disease. Nevertheless 44% of recruits developed antibody during their 12 weeks of training and as the overall incidence of pneumonia was 1.5%, about 1 infection in 30, was manifest as pneumonia. However there were more antibody rises in cases of "febrile and afebrile respiratory disease" than in recruits with no respiratory illness, but the majority of infections appeared to be asymptomatic. Infection was detected in all sections of the organization and throughout the period of the study. The agent was apparently a "poor spreader".

[This paper should be read by all interested in this subject.]

D. A. J. Tyrrell

McKERRON, C. B., OLDHAM, P. D. & THOMSON, S. **Antibiotics and the Common Cold.** *Lancet*. 1961, Jan. 28, 185-7.

This is a report of a controlled trial from the Pneumoconiosis Research Unit of the Medical Research Council. It was undertaken to test RITCHIE's hypothesis [this *Bulletin*, 1959, v. 34, 21 *bis*, 22] that small doses of antibiotics taken at the beginning of a common cold can prevent secondary bacterial invasion and so shorten the duration of symptoms. The subjects studied were: 138 ex-miners suffering from pneumoconiosis and some degree of bronchitis, and 55 normal adults (volunteers from the Unit).

Either dummy lozenges or active lozenges containing 15 mgm. tetracycline, or oxytetracycline, or chlortetracycline (depending on the sensitivity of the salivary organisms), were allocated at random to those reporting the earliest symptoms of a cold; the dosage was 3 lozenges daily for 3 days. The results were assessed on the basis of the disappearance of all symptoms of the cold when the subject reported on the 4th day. The proportion of first colds thus "cured" in both groups was similar, and on combining the results it was seen that 23% of the colds were cured in 3 days on dummy lozenges, and 50% on active lozenges. The difference is significant and Ritchie's hypothesis is thus confirmed.

There was no evidence that the antibiotics speeded the cure of illnesses starting in the chest. 6 months after the trial ended the proportion of subjects harbouring drug-resistant salivary organisms was found to be increased, but this drug resistance was found equally in those who had taken active and dummy tablets; the significance of the observation was thus uncertain.

The weight of evidence now strongly supports the idea that recovery from the common cold can be speeded by early treatment with antibiotics. The most suitable antibiotic and the optimal dosage remain to be determined.

H. Stanley Banks

SCHEID, W. **Mumps Virus and the Central Nervous System.** *World Neurology.* Minneapolis. 1961, Feb., v. 2, No. 2, 117-33. [41 refs.]

This article consists of a critical review of the literature on neurological complications of mumps. The incidence of these complications is difficult to assess as, especially in earlier literature, full investigations have not been carried out and cases of non-parotitic mumps have probably been missed. Differing rates of incidence are probably related more to these factors than to a change in the neurotropism of the virus. Accounts of neurological complications must be scrutinized before they are accepted as definitely due to mumps. [This is an excellent review of the subject, concerned mainly with the incidence, pathogenesis and clinical aspects of the neurological complications of mumps.] *A. B. Christie*

BÜRGIN-WOLFF, Annemarie, ROSSIER, R., SALZBERG, R. & BERGER, E. **Poliomyelitis: Klinische Befunde und Laboratoriumsergebnisse. Bedeutung von Doppelinfektionen und Beeinflussung der Kinderlähmung durch die Salk-Vaccination. [Poliomyelitis: Clinical Findings and Laboratory Results. The Significance of Double Infection and the Effect of Salk Vaccination on Infantile Paralysis]** *Schweiz. med. Woch.* 1960, Nov. 26, v. 90, No. 48, 1364-70, 4 figs. [20 refs.]

In investigations carried out in 1959 in Basle poliomyelitis virus was isolated from 96 children aged up to 15 years, including 33 with a clinical diagnosis of poliomyelitis, 23 with serous meningitis and 25 with other diagnoses. The remaining 15 were contacts. Type 1 virus was isolated from 56, type 2 in 4 and type 3 from 43 patients. 69 patients were also investigated serologically by means of neutralization and complement-fixation tests; by both methods together a diagnostic level of antibody to the type of virus isolated was found in 48 (about 75%). The patients who did not form antibody to their own type were mostly suffering from mild or asymptomatic infections. 4 children suffering from mild or moderate paralytic type 3 infection formed no type 3 antibody, and it was considered that this type is a poor antigen, and consequently that the absence of type 3 antibody does not exclude a diagnosis of poliomyelitis. 7 of 8 patients infected with 2 types of virus formed antibody to 1 type only. This partial lack of response was ascribed to interference between the 2 viruses. 44 of the patients investigated had received Salk vaccine during the 2 preceding years, of whom 5 developed paralytic poliomyelitis. It is finally pointed out that the persistence of antibody due to vaccination may cause difficulties in subsequent serological diagnosis.

D. J. Bauer

HASSAN, M. M. & HASEEB, M. A. **Poliomyelitis in Khartoum.** *J. Trop. Med. & Hyg.* 1960, Nov., v. 63, No. 11, 265-6.

An epidemic of poliomyelitis occurred in Khartoum in 1959, affecting children (4 months to 7 years of age, mostly 1½ to 3 years) and with its peak in August. 120

patients, most of whom were paralysed, were seen in the Children's Department of Khartoum Hospital. 35 specimens of faeces were sent to Johannesburg for isolation of virus, and 5 gave type 1, and 2 gave type 3; 4 showed Cocksackie viruses and 3 showed other (unknown) viruses. Blood from 20 patients (in the acute and convalescent stages) were tested for antibody; type 1 antibody was the most common, type 3 the next and type 2 the least.

This was the first epidemic to be observed in Khartoum, where the disease is endemic. The social and hygienic standards of the people are rapidly improving, and a change in the epidemiology of the disease may occur; immunization is strongly recommended for children.

Charles Wilcocks

LO MONACO, G. B. Una epidemia mista di infezioni da poliovirus tipo 1 e altri enterovirus. [Mixed Outbreak of Infections from Type 1 Poliovirus and other Enteroviruses] *Ann. d. San. Pubblica.* Rome. 1960, Nov.-Dec., v. 21, No. 6, 1445-68, 2 figs. [36 refs.] English summary.

The author here reports his findings in the laboratory investigation of an outbreak of poliomyelitis which was associated with other virus illness. The illness affected the adjoining villages of Pinzano, Petrognano, Pamino and Castelnovo in the rural district of Rufina, near Florence, during August-September, 1958. There were 53 cases in all, in an aggregate population of 1,129; 45 patients were under 11 years old. 23 were in Pinzano, where the first 3, and the only paralytic cases, occurred—a girl, aged 3 years, with onset on August 6 and paralysis of trunk and lower limbs; a boy, aged 18 months, with onset on August 11 and a temporary paresis of the lower limbs; and another boy, also aged 3, with onset on August 13 and facial and oculomotor paralysis. This last patient died before any laboratory investigations were possible. The 50 non-paralysed patients showed various combinations of the following signs and symptoms:—pyrexia, limb pains, pharyngitis, diarrhoea, vomiting, headache, rigidity of neck and abdominal aches.

The author carried out virological and immunological investigations on throat swabs and specimens of faeces and blood serum taken from the patients and from a number of contacts, which included (1) 23 of the 29 well children, aged 10 years or under, in Pinzano, of whom 5 were direct contacts of patients, (2) 15 adult contacts in Pinzano, (3) 7 contacts in Pamino and (4) 4 contacts in Petrognano. He used 2 kinds of cells for the tissue cultures. Of the 52 patients investigated, 23 (44%) yielded a positive culture—Polio type 1 in 14 (61%), ECHO (Pinzano 702, related to type 2) in 7 (30%) and Cocksackie B type 4 in 2 (9%). Both polio and ECHO viruses tended to remain in isolated foci and to spread only by direct contact over short distances. *J. Cauchi*

MAGOFFIN, R. L., LENNETTE, E. H., HOLLISTER, A. C., Jr. & SCHMIDT, Nathalie J. **An Etiologic Study of Clinical Paralytic Poliomyelitis.** *J. Amer. Med. Ass.* 1961, Jan. 28, v. 175, No. 4, 269-78, 1 fig. [16 refs.]

This is a most interesting aetiological study of illnesses diagnosed as paralytic poliomyelitis in 1955, 1956 and

1957 in California. 198 vaccinated and 160 non-vaccinated patients were studied. These represented 77% of the vaccinated and 7% of the non-vaccinated patients occurring in this area. Attempts were made at virus isolation and diagnosis by serological means.

It was found that poliovirus was much more likely to be implicated as the cause of severe than of mild disease. In the cases with minimal or mild paralysis there was either no evidence of poliovirus infection or evidence of infection with another enterovirus. There were in all 49 cases with good evidence of infection by a virus other than polio. 8 of these cases also had good evidence of poliovirus infection, making it very difficult to determine whether they were due to polio or to the other virus.

It was felt probable that, since the cases from which non-polioviruses were recovered were concentrated in the milder group of illnesses, the non-poliovirus was more likely to have been the aetiological agent. The agents that were implicated in the 41 instances where there was no good evidence of poliovirus infection were: Coxsackie B2 virus (3 cases); B4 (4); B5 (6); ECHO virus type 6 (1); unidentified ECHO viruses (11); mumps virus (12); herpes simplex virus (3); St. Louis encephalitis virus (1 case).

It was also found that the polioviruses were less often implicated as the cause of disease in people who had been vaccinated. Among non-immunized patients good evidence of poliovirus infection was found in 17% of the non-paralytic cases, 50% of the mild cases and approaching 100% in the severe cases. Non-poliomyelitis infections were associated either with non-paralytic disease or with minimal or moderate paralysis. In patients who had been vaccinated against poliomyelitis there was a similar increase in the percentage of cases associated with poliovirus infection as the severity increased but at all levels the incidence of poliovirus infection was considerably less than for the non-immunized. For example, among those with severe paralysis, virtually 100% of the non-immunized had evidence of poliovirus infection whereas 44% of those who had had 2 or more doses of poliovaccine were infected. Among the vaccinated patients with minimal to moderate degrees of paralysis, the reduction in poliovirus infections coincided with an increase in the percentage of non-poliovirus infections. Thus, in those with minimal paralysis, 52% of the non-vaccinated and 7% of those who had had 2 or more doses had good evidence of poliovirus infection. Similarly, 12% of the non-vaccinated and 45% of those who had had 2 or more doses of vaccine had evidence of a non-poliovirus infection.

The authors note that many of the mild and moderate cases might well not have been classed as cases of paralytic poliomyelitis if it had not been for the careful muscle evaluations that were performed and almost certainly these patients would have made, or did make, a good recovery. They also note that they have experienced no cases of severe paralysis due to a non-poliovirus although such cases have been reported by other workers (see, for example, STEIGMAN, *J. Mount Sinai Hospital*, New York, 1958, v. 25, 391). Although there is clear evidence from this study that the proportion of cases of paralytic disease due to non-polioviruses is higher in vaccinated individuals there is no evidence that the absolute incidence of these diseases is higher in the vaccinated segment of the population.

[In a letter commenting on this paper A. J. STEIGMAN (*J. Amer. Med. Ass.*, 1961, v. 176, 550) thinks there may be 3 reasons why no serious cases of paralysis due to non-poliovirus were found:

- (1) The study referred mainly to 1956 (73% of patients examined),
- (2) No examination of post-mortem materials were made, and
- (3) Suckling mice were not used routinely for Coxsackie virus infection.] A. J. Beale

KUBRYK, D. **Paralytic Poliomyelitis in Canada, 1959.**
Canadian J. Pub. Health. 1960, Oct., v. 51, No. 10, 389-99, 3 figs.

In 1959, Canada had a very severe outbreak of paralytic poliomyelitis with a total of 1,870 cases and 178 deaths. All the provinces except Manitoba had high incidence rates of poliomyelitis, the overall rate for the country being 10.7 per 100,000. The hardest hit areas were Newfoundland with 31 cases per 100,000 of the population and Quebec with 23.2. 3 patterns of age distribution were noted. First, in Newfoundland, an epidemic of infantile paralysis occurred with 85% of the cases in the 0-9 year age-group, those under 5 years accounting for 66%. In Quebec there were about equal numbers of cases in the 0-4 and in the 5-9 year age-groups with the other 30% of the cases occurring in teenagers and adults. This is the pattern that was observed in Canada before the mass use of vaccine. In the remaining provinces the pattern of incidence was similar to that recorded in the years since vaccination in the United States with a concentration of cases in the pre-school age group—40% in the 0-4 year age-group, 20% aged 5-9, 8% aged 10-19 and 31% in the adult age group.

The fatality rate was lowest in the 1-4 year age-group and highest in the 40 and over age-group. In fact, the youngest patient, who was 7 weeks old, and the oldest, aged 72, both died. The incidence was higher in males than in females, except in the age-group 20-34 where female cases exceeded males. The paralytic attack rate in pregnant women was no greater than in non-pregnant women of the same age. In Quebec there were 20 cases in pregnant women with 3 deaths but the case fatality rate was no higher than in non-pregnant females of the same age. In an analysis of just over 1,000 cases, 33% made a complete recovery, 17% had muscular weakness only and 40% were still paralysed at the time of follow-up; 10% were dead. Laboratory studies showed that 85% of the cases were due to type 1 poliovirus. A few cases yielded type 2 or type 3 virus.

The majority of the patients (72%) were unvaccinated but a large number (11.2%) had been given 3 or more doses of vaccine. The effectiveness of the vaccine was estimated from the estimated vaccination status of the Canadian population in June 1959. It was found that the effectiveness was 87% in the 0-4 year age-group, 97% at 5-19, which was the best vaccinated age-group, and 74% at 20-39 years, the worst vaccinated. A. J. Beale

WINGATE, M. B., MELLER, H. K. & ORMISTON, G.
Acute Bulbar Poliomyelitis in Late Pregnancy.
Brit. Med. J. 1961, Feb. 11, 407-9. [14 refs.]

Signs of bulbar poliomyelitis appeared in a multi-gravida aged 42 about a week before her confinement was due. Her respiratory difficulty and general condition rapidly deteriorated, and 4 hours after admission her heart suddenly stopped beating. While respiration was kept going by intermittent positive pressure through a face mask, her heart was massaged, caesarean section performed and a female infant weighing 5lb. 11oz. was delivered. By this time the mother was dead. Type 1 virus was isolated from her stools and tissues at necropsy.

The infant thrived and did not develop paralysis. She passed type 1 poliovirus in her stools on the 5th day and for the next 12 weeks. Gamma globulin 500 mgm. given on the day of birth may have protected her nervous system during the viraemic phase. It did not interfere with the silent process of active immunization, as shown by a steady rise in her type 1 antibody titre.

H. Stanley Banks

ILLINOIS MED. J. (Reprinted from) 1960, Aug. & Sept., v. 118, Nos. 2 & 3, 19 pp., 2 figs. **The Present Status of Polio Vaccines** [RATNER, H. (Moderator); COX, H. R.; GREENBERG, B. G.; KLEINMAN, H.; MEIER, P. (Panelists)]. **Bibliography and Notes prepared by H. RATNER**, 16 mimeographed pp. (available on request).

A panel discussion on the present status of poliovaccines was held in Chicago on May 26th, 1960. 2 of the panellists, Dr. Ratner and Professor Meier, have been critics of Salk poliovaccine since its inception. Professor Greenberg and Dr. Kleinman have been concerned with the evaluation of poliovaccine effectiveness and Dr. Cox is responsible for the development of attenuated poliovirus vaccine. Kleinman has also been concerned with field trials of Lederle attenuated poliovaccine. The burden of the argument is that killed poliovaccine has been a failure and that a change to a living vaccine should be made.

Ratner notes that poliomyelitis incidence has increased from the 1957 level in 1958 and 1959, and that substantial numbers of cases occur in the triply vaccinated. Greenberg points out some fallacies in the assessment of poliovaccine effectiveness. First, the requirements have altered to increase safety but it is thought that poliovaccine potency decreases following the introduction of a second filtration step. [In the reviewer's experience of making killed vaccine it is clear that the quality of the filtration vitally affects safety but that with suitable precautions no potency need be lost.] The report of the Poliomyelitis Surveillance Unit of December 7th, 1955, is severely criticized because the numbers of children were taken from the 1950 census and no allowance was made for increases in the population. Also, children were considered as vaccinated regardless of whether they were vaccinated early or late in the year. This diminishes the rate in the vaccinated owing to swelling the vaccinated population with those who were vaccinated late in the

year after having escaped clinical infection earlier. Differences in diagnostic criteria for non-paralytic and paralytic cases introduced as a result of the 1954 killed poliovaccine trial are thought to be the major cause of the fall in incidence of reported poliomyelitis in 1957. [Most analyses of killed poliovaccine effectiveness allowing for these factors have showed it to be at least 80% effective.]

Kleinman, who had previously estimated killed poliovaccine to be very effective, is now dubious because of the increase in numbers of paralytic poliomyelitis. He confesses himself unable to decide whether the vaccine is or is not effective.

Meier reiterates his early fears about killed poliovaccine safety and the adequacy of the tests. He is uneasy about the propaganda effort to promote killed poliovaccine. Experts, he contends, have doubts but in the newspapers the killed vaccine is represented as safe and very effective.

Cox and Kleinman describe the development and use of attenuated poliovaccine mainly in Latin America and Minnesota. They believe the vaccine to be safe and effective in producing antibodies and therefore most likely to be effective in preventing poliomyelitis. Ratner, summing up, concludes that, if killed poliovaccine is safe and highly effective, licensing of living vaccine is not urgent. The panel's view is that this proposition is not proven and that a living vaccine is an urgent necessity.

[The failure of killed poliovaccine has mainly been due to failure to achieve satisfactory acceptance of the vaccine. It is hoped that this problem will be overcome by an oral vaccine. One argument used in favour of living vaccine is the uniform satisfactory results with living vaccines in the veterinary field. A review by PRIER, *J. Amer. Vet. Med. Ass.*, 1960, v. 137, 577, is not quite so enthusiastic.]

A. J. Beale

RHODES, A. J. **Public Health Aspects of Live Poliovirus Vaccines with particular reference to Canada.** *Canadian J. Pub. Health.* 1961, Feb., v. 52, No. 2, 45-54. [34 refs.]

In this paper Professor Rhodes gives an authoritative account of the present position of live poliovaccination, especially in Canada where he is the Chairman of the National Technical Advisory Committee on Live Poliovirus Vaccines. In Canada there has been a favourable experience with Salk vaccine; the effectiveness has been estimated at about 80%. However, during 1959 there was an extensive epidemic of poliomyelitis in Canada which was mainly in the unvaccinated or incompletely vaccinated persons. 193 patients (11% of the total number) had received 3 doses of killed vaccine.

The chief advantages claimed for live poliovaccine are as follows: (1) the vaccines are simple and cheap to administer; (2) the cost of production should also be low; (3) the vaccine induces a state of resistance in the gastrointestinal tract as a result of intestinal multiplication; (4) antibody develops quickly as a sequel to gastrointestinal infection. Because of the rapid development of antibodies and the gastrointestinal resistance it is thought that the vaccine should be effective under epidemic conditions. It is pointed out that the validity of

some of these claims remains to be proved in practice and also that certain other factors may lower the efficacy of the vaccine in the field, for example, interference either between the various attenuated strains or from other enteroviruses may occur.

The record of safety of living poliovaccine is excellent but continued trials of the safety of the vaccine under Canadian conditions are being carried out, particularly with reference to the genetic stability of the virus on passage in man and also its effect on a community basis during the winter months in Canada.

It is noted that the efficacy of the vaccine has not been rigorously proved, as has been done for Salk vaccine, but the evidence so far coming from the field, both from the epidemiological investigations and also from the serological results, indicates that the vaccine will prove effective. It is considered that the administrative problems would be considerably easier if the vaccine could be given as a trivalent mixture but it is noted that this may lead to interference between the strains and the necessity to give more than one dose. The idea of eradicating the disease-producing agent, the poliovirus, from a community by means of blanketing the population with live viruses is mentioned. It is considered that Newfoundland might prove to be an appropriate place to test the possibilities of this approach.

Finally, the main recommendations of the Canadian Advisory Committee are listed. These are in summary: (1) that live poliovirus poliovaccination should be adopted in the face of an epidemic; (2) that vaccination with attenuated viruses should be used as a research project for those failing to respond to Salk vaccine; (3) that trials be undertaken in the winter to investigate the use of varying dosages of virus, various schedules, the relative value of trivalent and monovalent vaccines, duration of faecal excretion, occurrence of viraemia, antibody response, ease of spread of virus to contacts, genetic stability of virus on transfer in the human host; (4) the need for adequate supervision, including laboratory facilities, in the study of live poliovirus programmes is stressed; (5) at present the incorporation of live poliovirus vaccine into the Public Health programme is not recommended; (6) the Committee believes that there will be a place for both living and killed poliovaccines in the immunization programme; (7) the continued use of Salk vaccine is endorsed and encouraged.

A. J. Beale

KRUGMAN, S., WARREN, J., EIGER, M. S., BERMAN, P. H., MICHAELS, R. M. & SABIN, A. B. **Immunization with Live Attenuated Poliovirus Vaccine.** *Amer. J. Dis. Children.* 1961, Jan., v. 101, No. 1, 23-8, 1 chart. Discussion 28-9.

400 infants were given Sabin's strains of living poliovaccine by mouth, according to 11 different schedules, within a few hours of birth. Virus isolations were attempted about 5 days later and antibody studies were carried out 3 months later. The schedules were of 2 sorts, some infants being given type 1 only and the others all 3 types. It was found that virus excretion

occurred in about 80-90% of the infants but in those given all 3 types type 2 predominated. Young infants given vaccine by mouth were as likely to be infected as those who had vaccine swabbed on to the fauces. Antibody responses were difficult to assess because of maternal antibodies. An infant was considered to have responded if the antibody titre rose, remained the same or fell only 2-fold in the 3 months. These criteria are based on results obtained with 19 unvaccinated infants whose maternal antibodies fell 4- to 128-fold in the same period. The response for those given type 1 only was about 30% but varied according to schedule. It was 55-77% in those with maternal antibody titres of 1 in 64 or less. Those given all 3 types made even poorer responses except for type 2 which were of about the same order. It was concluded that more time is required to assess the effect of the vaccine in this age-group, because of the masking effect of maternal antibody, and that the vaccine strains must be given separately. 2 dose levels of vaccine were used, undiluted ($10^{7.6}$ TCD₅₀ for type 1) and 1 in 10. The results were slightly, though probably insignificantly, worse for the 1 in 10 dilution than for the undiluted vaccine.

A. J. Beale

CABASSO, V. J., JUNGHERR, E. L., MOYER, A. W., ROCA-GARCIA, M. & COX, H. R. **Oral Poliomyelitis Vaccine, Lederle—Thirteen Years of Laboratory and Field Investigation. An Interim Review.** *New England J. of Med.* 1960, Dec. 29, v. 263, No. 26, 1321-30. [33 refs.]

This paper reviews experiences with Lederle attenuated poliovaccine. This has been used either as monovalent vaccine or as a trivalent mixture on over 1 million people. There have been no cases of nervous disease attributable to the vaccine, whereas several hundred cases might have been expected from the exposure of a similar estimated number of susceptibles to virulent poliomyelitis virus. [There is no mention or analysis of the cases which occurred in Dade County and Berlin at the same time as the Lederle vaccine was given to these communities.] The antibody response to all 3 types of virus has proved excellent, usually over 90% if all 3 types are given separately, although under some conditions—in adults or children exposed to other enteroviruses—the rate of conversion may fall below 50%. The response to trivalent vaccine was slightly less favourable, being around 70% although varying according to type and the community studied. The viruses isolated from persons who received the vaccine by mouth, or from contacts to whom virus spread had greater neurovirulence for monkeys than the vaccine strains. Thus the intracerebral paralytic rate of viruses isolated from faeces exceeded 5% for type 1 and 12% for type 3. The rate for viruses isolated from contacts was not, however, higher than that for viruses from persons given the vaccine orally, suggesting that rapidly increasing virulence on human passage did not occur.

A. J. Beale

ŽÁČEK, K., ADAM, E., RADKOVSKÝ, J., VONKA, V., VANĚČKOVÁ, Nina, ŘEŽÁCOVÁ, Dagmar, JANDA, Z. & ADAMOVÁ, Vlasta. **Repeated Serological Surveys performed in the General Population of Czechoslovakia before and after the Vaccination of Children with Inactivated and Live Poliovirus Vaccine.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 453-69, 11 figs. [10 refs.]

In Czechoslovakia a programme of poliomyelitis vaccination with Salk type vaccine was initiated in 1957. Because of a shortage of vaccine 0.2 to 0.3 ml. of vaccine was given intradermally with 2 primary doses and a booster later. In one area, Plzen, about 60% of the children received a fourth 1 ml. dose of vaccine. In 4 areas Sabin's vaccine was given to children aged 2-8 years. Serological studies were carried out in January to March 1957, and November 1958, after the Salk vaccine programme, and in March 1959, after the use of Sabin vaccine. Before vaccination in the Usti region, 51% of the 1-year-old and 13% of the 3-year-old children were triple negative and after 3 doses of Salk vaccine 33% were triple negative at 1 year and 27% at 3 years. In 1959, after the use of Sabin vaccine, 35% were triple negative at 1 year and 13% at 3 years. These results are taken to show the great superiority of living poliovirus vaccination. *A. J. Beale*

BURIAN, V., VOJTOVÁ, Helena, ŽÁČEK, K. & VANĚČKOVÁ, Nina. **The Spread of Polioviruses in the Population vaccinated with Live Attenuated Polioviruses in comparison with the Non-Vaccinated Population.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 470-76, 2 figs.

Faeces were examined for enteroviruses before and at varying times after the use of Sabin attenuated poliomyelitis vaccine both in areas in Czechoslovakia where the vaccine was used and in control districts. Before the use of vaccine the incidence of poliomyelitis viruses was low. The vaccine strains were given in the order types 1, 3 and 2. After vaccination the higher incidence of poliomyelitis viruses did not persist for long. By 4 months for all types the incidence was no higher than in control areas. Samples taken during the height of the following poliomyelitis season (September-October 1959) revealed no higher incidence than in control districts. The incidence was, in fact, lower but the numbers were too small for any definite significance to be ascribed to the difference. *A. J. Beale*

SANTOPADRE, G., CASAROSA, S., RUSCHI, A. & ZERBONI, R. Sulla risposta anticorpale a vaccino antipoliomielitico (tipo Salk) in un gruppo di bambini della Provincia di Pisa. **[The Antibody Response to Poliomyelitis Vaccine (Salk Type) in a Group of Children in the Province of Pisa]** *Riv. Istituto Sieroterap. Ital.* 1960, Sept.-Oct., v. 35, No. 5, 575-89. English summary (9 lines).

An investigation has been made of the antibody response in 285 randomly selected children aged from 1 to

14 years and resident in the province of Pisa who were vaccinated in 1958-59 with Salk-type poliomyelitis vaccine. Sera were collected before vaccination and 1-2 months after the third injection; the titres of neutralizing antibody to the 3 types of virus were determined, and the results are presented in detail in a series of tables, together with a statistical evaluation. Type 1 antibody appeared in 88 of 152 subjects in whom it was absent before vaccination, and type 2 in 100 of 131 and type 3 in 75 of 161 respectively; the 3 types of antibody appeared in 27, 50 and 25 respectively of 77 subjects who were triply negative before vaccination. *D. J. Bauer*

MORRONE, G., NUNZIATA, B., PICCIOTTO, L. & BRANCATO, P. Risposta anticorpale del lattante al vaccino antipoliomielitico. **[Antibody Response to Poliomyelitis Vaccine in Young Infants]** *Riv. Istituto Sieroterap. Ital.* 1960, Sept.-Oct., v. 35, No. 5, 590-602, 3 graphs. [14 refs.] English summary.

The authors have investigated the antibody response to 3 doses of Salk-type poliomyelitis vaccine in 45 infants aged between 50 and 120 days at the time of the first injection; in 23 instances the vaccine was mixed with aluminium phosphate before injection. Examination of blood samples taken before vaccination and after the 2nd and 3rd doses revealed the development of satisfactory titres of neutralizing antibody to type 1 virus in 41, type 2 in 43 (of 44) and type 3 in 43 infants. No essential difference could be observed in the groups treated with vaccine containing aluminium phosphate. In those infants who lacked maternal antibody before vaccination, type 1 antibody appeared in all of 22, type 2 in all of 18 and type 3 in 26 of 27. *D. J. Bauer*

PERKINS, F. T., YETTS, Risha & GAISFORD, W. **Poliomyelitis Immunization in Infants in the Presence of Maternally Transmitted Antibody.** *Brit. Med. J.* 1961, Feb. 11, 404-6, 3 figs.

The authors have previously shown that maternal antibody interferes with the response of infants to killed poliomyelitis vaccine. Not only does it mask the interpretation which can be overcome by observing the effect of a booster dose but also it inhibits the production of antibody [this *Bulletin*, 1959, v. 34, 735, 736]. The authors have found that giving 3 primary doses elicits a much better response than 2 doses in children aged 4, 6 or 9 months [*ibid.*, 1960, v. 35, 56]. They are keen to employ poliovaccination early in life and therefore have inoculated younger infants aged 1, 5 and 9 weeks with 3 primary doses each of 2 ml.

In this paper they report the responses of infants given 3 primary doses at 1 week, 4 months or 6 or 9 months old at the beginning of the primary course to a booster dose 12-16 months later. Children that showed a rise in antibody titre between the end of the primary course and before the booster were excluded. Most children given the primary course at 1 week lacked antibodies at the time of the booster dose, especially for type 1, but afterwards, out of 22 children studied, 7, 1 and 3 had

titres of less than 1 in 128 against types 1, 2 and 3 respectively. Only 3 children had no antibodies (less than 1 in 8) to type 1, and 2 to type 3. The responses were better in children aged 4 months when first vaccinated. All had titres of 1024 or better for type 2 and 256 or better for type 3. 3 out of 22 children had titres of less than 128 to type 1, and all except 1 child made a booster response. The results in children aged 6 or 9 months were essentially the same. Only 2 out of 16 children failed to have titres of 1 in 128 against all 3 types. These 2 had titres of 1 in 16 against type 1. Both these children were 9 months old at the time of primary vaccination. The children given the primary course at 9 months made poorer responses on the whole. The batch of vaccine used for the 9-month-old children was presumably of lesser potency than that used for the 6-month-old infants. The authors are encouraged by these results to think that satisfactory immunization against poliomyelitis of infants at 1 week is an attainable goal.

A. J. Beale

WOODWARD, T. E., McCrUMB, F. R., Jr., CAREY, T. N. & TOGO, Y. **Viral and Rickettsial Causes of Cardiac Disease, including the Coxsackie Virus Etiology of Pericarditis and Myocarditis.** *Ann. Intern. Med.* 1960, Dec. 15, v. 53, No. 6, 1130-50, 5 figs. [68 refs.]

This is a review of the viral and rickettsial causes of cardiac diseases illustrated with examples from the authors' experience. Coxsackie B virus is now a well-recognized cause of neonatal myocarditis and 2 more fatal cases are described, and in addition, a severe but not fatal case, probably due to Coxsackie B2. Cases of myocarditis, probably due to influenza and poliomyelitis virus, and one of myocarditis due to Rocky Mountain spotted fever are also described. These reports show that aetiological studies on patients with myocarditis are well worth while, and similarly the aetiology of pericarditis is now more frequently ascertainable. 3 cases of Coxsackie B virus pericarditis were discovered in studies on 14 patients and short reports of 2 of them are presented. A fatal case, due to influenza virus, is described, in which the virus was isolated directly from the pericardial fluid.

[This is an interesting article but is a far from complete review of the subject.]

A. J. Beale

MAGOFFIN, R. L., JACKSON, E. W. & LENNETTE, E. H. **Vesicular Stomatitis and Exanthem. A Syndrome Associated with Coxsackie Virus, Type A16.** *J. Amer. Med. Ass.* 1961, Feb. 11, v. 175, No. 6, 441-5. [11 refs.]

The authors report on 33 illnesses in California characterized by stomatitis and, in some patients, by a vesicular rash, mainly on the hand and feet. Of 15 cases studied, 10 yielded Coxsackie virus type A16 from the faeces and serological evidence of infection: 1 gave serological evidence of infection with the same virus and 1

yielded Coxsackie virus type A4 from the faeces: in 3 cases virological results were negative.

A. B. Christie

LANE, A. J. (for HARRISON, R. J.). **Acute Non-Specific Pericarditis associated with High Titres to a Coxsackie Group B₄ Virus.** *Proc. Roy. Soc. Med.* 1961, Mar., v. 54, No. 3, 232-4 (Clin. Sect. 6-8). [16 refs.]

Report of a case.

DARDANONI, L. & ZAFFIRO, P. **Alcuni casi di reinfezione da virus ECHO 7. [Cases of Reinfection with Type 7 ECHO Virus]** *Riv. Istituto Sieroterap. Ital.* 1960, Sept.-Oct., v. 35, No. 5, 564-74, 5 figs. English summary.

During a continuous study of enterovirus infection carried out over a period of 1 year on 41 children aged up to 3 years who were inmates of an institution, the authors observed 5 cases of reinfection with type 7 ECHO virus. In 2 subjects the virus was isolated from rectal swabs shortly after admission to the institution and again after 13 and 14 months respectively, the second isolation being accompanied by a rise in titre of neutralizing antibody up to greater than 1280. In the remaining 3 subjects the reinfection was confirmed by isolation of the virus, but the initial infection was inferred from the presence of neutralizing antibody in titres of 20-160. During the period of observation 2 outbreaks of type 3 poliomyelitis infection occurred, but no instance of reinfection was observed.

D. J. Bauer

SOLT, Katalin & VEDRES, I. **Regional Distribution and Characteristics of Viral Hepatitis in Hungary during the Period 1952 to 1957.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 243-50, 7 figs. [10 refs.]

This is an epidemiological study of the distribution of viral hepatitis in the urban and rural districts of Hungary during a period of rising incidence, 1952-57. Inadequate data seem to have led to some curious findings; for example, that the morbidity of both viral hepatitis and typhoid fever was higher in towns provided with a water and sewage system than in those without them. This is said to suggest the importance of person to person transfer of both diseases. However it is stated that there is great variety in the extent of drainage provided in towns with a sewer system.

[It would seem to be unsound to base any conclusion on the aggregation of data from such areas. Moreover the term "viral hepatitis" includes both the infectious and syringe-transmitted variety, and, as the authors state, "the role of extensively used injection therapies . . . by means of not always correctly sterilized instruments" cannot be disregarded.]

H. Stanley Banks

FAVEZ, G., BONSTEIN, H. & PACHE, D. Répercussion de l'hépatite virale sur le pouvoir d'acétylation du foie. [Effect of Viral Hepatitis on the Capacity of the Liver to Acetylate] *Schweiz. med. Woch.* 1960, Dec. 17, v. 90, No. 51, 1467-9, 3 figs. [20 refs.]

The acetyl residue has a considerable part to play in the metabolism of the liver. It is involved in the breakdown of carbohydrates, proteins and fats, the synthesis of cholesterol, porphyrin, fatty acids and glucose, and it is used in the liver metabolism of the sulphonamides and of para-aminobenzoic acid (PAB). The measurement of acetylated PAS can therefore be used as a liver function test. The authors gave 11 patients, who were suffering from viral hepatitis, 20 gm. of sodium PAS intravenously in 500 ml. distilled water given during 1 hour. For 8 weeks after the onset of the hepatitis the acetylated PAS level in the blood measured after 2 hours was considerably lower than that found in normal controls. However, values obtained after 4-6 hours were within normal limits. These results suggest that the impairment of the liver function is due to an inability to perform a rapid acetylation of PAS. *H. Lehmann*

SANECKI, M. Odra w Polsce w latach 1919-1959 na tle sytuacji światowej. [Measles in Poland during 1919-1959 as compared with the World Situation] *Przegląd Epidemiol.* Warsaw. 1961, v. 15, No. 1, 41-52, 5 figs. [18 refs.]

The English summary appended to the paper is as follows:—

"A statistical analysis was made of the epidemiological situation of measles in Poland against the background of the world situation. The statistical data on morbidity and mortality may be treated as provisional data. A distinct improvement in registration is noted from 1961. Along with the large rise in morbidity, mortality due to measles in Poland shows a steady decline. The highest mortality is to be noted in the 0-4 year-old age group. A further lowering of mortality is possible through the extensive use of gamma globulin in this age group. Shifting morbidity to later years decreases the risk of death."

ZHDANOV, V. M. & FADEEVA, L. L. The Problem of the Development of a Measles Vaccine. *Problems of Virology.* London. 1959, v. 4, No. 5, 43-50. [13 refs.] [Translated from Russian.]

The authors have developed an attenuated strain of measles virus by prolonged passage in primary explant cultures of human embryo lung tissue and subsequent growth in the allantoic cavity for production purposes. In trial vaccinations with this material carried out on several hundred children, however, an insufficient degree of protection was obtained, and the Edmonston and Wright strains of measles virus were therefore used in further work, together with a Russian strain from another source.

315 children aged 1-4 years, vaccinated intranasally by dermal scarification or subcutaneously with tissue culture fluid containing these strains of virus developed only mild reactions consisting of nasal catarrh between the 7th and 11th days after vaccination. 19 children who were closely exposed to measles infection 1-6 months after vaccination all developed a mild attack of the disease. *D. J. Bauer*

CAMPBELL, M. Place of Maternal Rubella in the Aetiology of Congenital Heart Disease. *Brit. Med. J.* 1961, Mar. 11, 691-6, 1 fig. [30 refs.]

In a general review of the literature the author seeks to answer 4 questions:— (1) what is the risk to the child after maternal rubella during pregnancy? (2) when the heart is affected what malformations are most common? (3) what proportion of congenital heart disease is due to maternal rubella? (4) how important are other infections, viral or bacterial? On the first question he cites, as both sufficiently detailed and accurate, the prospective studies of LAMY and SEROR in Paris [this *Bulletin*, 1956, v. 31, 886], BRADFORD HILL *et al.* [*ibid.*, 1958, v. 33, 551] and the British Ministry of Health report by MANSON *et al.* [*ibid.*, 1961, v. 36, 579]. In view of the variability in their results he is compelled to take a rather wide range for the risk of a malformation (any type) occurring, viz. between 30 and 70% during the first 4 weeks, 25 and 55% during the second 4 weeks, 20 and 40% during the third 4 weeks and 10 and 25% during the fourth 4 weeks. Possibly the lower figures are generally more accurate and the higher figures are found in particular epidemics, e.g., the 1940 epidemic appears to have been particularly potent. The problem of a therapeutic abortion therefore remains a difficult one for the doctor during the first 3 months of pregnancy and must be settled according to individual circumstances. After the third month the question does not arise.

153 reported cardiac malformations show the relative frequency of congenital heart diseases after maternal rubella to be persistent ductus arteriosus 58%, ventricular septal defect 17.6%, Fallot's tetralogy 7%, atrial septal defect 6.6%, pulmonary valvular stenosis 6%, other types 4.6%.

Estimates by various workers of the proportion of cases of congenital heart disease that is attributable to maternal rubella range from 1.2 to 8%. The author's experience favours a low figure and he thinks it most unlikely that it exceeds 3 or 4% at the most. That other viral infections as well as rubella can cause some congenital malformations seems to be established, but it is most unlikely that they cause any substantial amount of congenital heart disease. Further prospective investigations are to be desired. *A. Bradford Hill*

LOVRIC, V. A. A Slide Test for the Diagnosis of Glandular Fever. *Lancet.* 1961, Jan. 21, 142-3. [12 refs.]

A simpler technique than the differential absorption test is proposed for determining the specificity of the Paul-Bunnell reaction in glandular fever. It is based on

the finding [WOLLNER, this *Bulletin*, 1956, v. 31, 699] that a proteolytic enzyme, papain, inactivates the receptors on sheep erythrocytes for the antibodies associated with glandular fever. The time taken to agglutinate papain-treated sheep red cells with the patients' serum is, therefore, always longer (by at least 15 seconds) than the time required for agglutination of native sheep red cells with the same serum. On the assumption that an agglutination titre of 1:80 or more has been found in a suspected case of glandular fever, a simple slide test with both native and papain-treated sheep erythrocytes can replace the time-consuming absorption test for specificity.

The slide test is performed at room temperature. A drop of a 20% suspension of washed sheep erythrocytes is placed on each end of a clean, dry, microscopic slide. A drop of papain solution (prepared and stored as described) is mixed with one of these drops, and a drop of physiological saline with the other. After 3 minutes one drop of the patient's serum is added to each end of the slide, and the stop-watch started. The slide is rocked gently and the time when macroscopic haemagglutination is observed is recorded.

68 normal sera and 302 sera from various diseases, including 28 from glandular fever, were examined. With the glandular fever sera the papain-treated erythrocytes always showed a delay in the onset of agglutination of at least 15 seconds when compared with the time of onset of agglutination of the native erythrocytes. A typical example gave the following figures: presumptive test titre 1:896; titre after absorption with (a) ox erythrocytes 1:7, (b) guineapig kidney 1:896; time to onset of agglutination in the slide test of (a) native erythrocytes 26 seconds, (b) papain-treated erythrocytes 120 seconds.

H. Stanley Banks

ANTHONISEN, P., STEINICKE, O. & THOMSEN, A. C. **Thrombocytopenic Purpura complicating Infectious Mononucleosis.** *Danish Med. Bull.* 1960, Dec., v. 7, Nos. 7/8, 215-17. [27 refs.]

According to some authors, moderate thrombocytopenia and slight haemorrhagic complications are frequently observed in infectious mononucleosis. Severe complications of this nature are rare, and the authors were able to find only 26 recorded cases. They report a further case in a boy of 7 years. He had lymphatic gland enlargement, palpable spleen, and a characteristic blood picture, but the Paul-Bunnell reaction was negative. The haemorrhage took the form of violent epistaxis, petechiae and purpura, and was observed within a few days of the onset of mild febrile symptoms. The thrombocyte count was found to be very low (3,000 per cmm.) and the bleeding and coagulation times were much prolonged. Recovery was rapid; the thrombocyte count was normal (336,000) by the 9th day of disease. Prednisone treatment was given but was not thought to have had any effect.

[It would be interesting to have confirmation of the finding that moderate thrombocytopenia is common in infectious mononucleosis. This could easily be done if a thrombocyte count were made a routine test on the establishment of the diagnosis in a large series. Indirect evidence might thus be gained in support of the hypothesis of antibody formation of various kinds in this disease, and specific antibodies against red cells, platelets and perhaps neural elements could then be looked for. FREEMAN and WAKEFIELD (*Lancet*, 1958, v. 2, 883) demonstrated a substance that agglutinated blood platelets in the serum of one patient.]

H. Stanley Banks

Bacteriology and Immunity

The order in this section is:—General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. Their titles and page references are cited below in the appropriate sub-divisions of this section.

GENERAL

BOWEN, T. J., DAGLEY, S., SYKES, J. & WILD, D. G. **Nature of the Ribosomes present in Bacteria and Yeast: a Re-Appraisal.** *Nature.* 1961, Feb. 25, v. 189, 638-40, 2 figs.

Particles of ribonucleoprotein (ribosomes) form a major constituent of bacterial cytoplasm and give rise to two fast-moving boundaries (30S and 50S) in the ultracentrifuge. Larger species such as 70S may be formed by aggregation when the concentration of magnesium ions

is raised and phosphate ions are excluded and it has generally been assumed that particles of this size exist inside the bacterial cell and have specific biochemical functions. In order to stabilize such large particles it is usual to prepare extracts for sedimentation with tris buffer containing magnesium acetate.

The authors examined concentrated cell extracts of *Escherichia coli* and *Bacillus cereus* under conditions approximating as closely as possible to those prevailing within the intact cell and were unable to detect ribosomes

sedimenting faster than the 30S and 50S fractions. Larger species were detected in more dilute extracts containing magnesium acetate but not in similar extracts in phosphate buffer and the authors suggest that the addition of magnesium acetate to extracts in order to "stabilize" large ribosomes is arbitrary and may be misleading. Similar experiments with the yeast *Saccharomyces cerevisiae* showed that the principal boundary evident in the ultracentrifuge was due to an 80S ribosome as has been reported by other workers.

John R. Norris

MAY, P. S., WINTER, J. W., FRIED, G. H. & ANTOPOL, W. **Effect of Tetrazolium Salts on Selected Bacterial Species.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 364-6. [16 refs.]

Tetrazolium salts are surface-reducing agents which have some structural resemblance to the triphenylmethane dyes. It is known that living Gram-positive bacteria are generally more permeable to these dyes and more susceptible to their bacteriostatic action than Gram-negative bacteria. The observations recorded in this paper show that Gram-negative bacteria are more resistant than Gram-positive organisms to the inhibitory effect of the tetrazolium salts on bacterial growth. Di-tetrazolium compounds, such as "blue-tetrazolium", have a greater lethal effect on bacteria than the mono-tetrazolium salts, such as triphenyl tetrazolium chloride. Increased resistance to the lethal effect of the tetrazolium compounds as shown by Gram-negative bacteria is generally reflected in the degree of reduction of the tetrazolium salt and the intensity of the coloured formazans resulting from this.

H. J. Bensted

KAZANTZIS, G. **Air Contamination from High-Speed Dental Drills.** *Proc. Roy. Soc. Med.* 1961, Mar., v. 54, No. 3, 242-4 (Sect. Odontol. 4-6), 3 figs.

Air sampled near the head of a patient who was having a tooth drilled with a high-speed drill used without a water spray showed an oil concentration of 0.62 mgm. per cu.m., with an oil droplet count of up to 180 per cc. The calcium concentration was 0.047 mgm. per cu.m. Higher levels than this were reached when an air syringe was used to blow the debris out of a cavity drilled in the conventional way. No evidence could be obtained of dispersal of significant numbers of mouth bacteria.

R. E. O. Williams

GILLISEN, G., SCHOLZ, H. & DEHNERT, Christa. **Die Behandlung von Keimsuspensionen mit Ionen-austauschern. [The Treatment of Microbial Suspensions with Ion Exchangers]** *Arch. f. Hyg. u. Bakt.* 1961, Mar., v. 145, No. 2, 145-52.

The English summary appended to the paper is as follows:—

"It is possible by means of an anion exchanger to eliminate cells of bread yeast, staphylococci, and spores of bacilli from the aqueous suspensions. In contrast, cation exchangers have a negligible effect, or none at all. The efficiency of anion exchangers varies both with respect to the concentration of the suspended cells as well as the species."

OBAYASHI, Y., OTA, S. & ARAI, S. **Some Factors affecting Preservability of Freeze-Dried Bacteria.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 77-91, 3 figs. [12 refs.]

SCHAEGLER, R. W. & DUBOS, R. J. **The Susceptibility of Mice to Bacterial Endotoxins.** *J. Exper. Med.* 1961, Mar. 1, v. 113, No. 3, 559-70. [18 refs.]

"Albino mice (Rockefeller NCS strain) raised and maintained free of ordinary bacterial pathogens, as well as of intestinal *Escherichia coli* and of *Proteus bacilli*, were found to be highly resistant to the lethal effect of bacterial endotoxins.

"When newborn mice of this NCS colony were nursed by foster mothers from another colony raised under ordinary conditions (SS colony from which the NCS colony was derived), they acquired the intestinal flora of the latter animals and became susceptible to the lethal effects of endotoxins.

"NCS adult mice could be rendered susceptible to the lethal effect of endotoxins by vaccination with heat killed Gram-negative bacilli. The susceptibility thus induced exhibited a certain degree of specificity for the bacterial strain used in vaccination.

"Although untreated NCS mice were resistant to the lethal effect of endotoxins, they proved exquisitely susceptible to the infection-enhancing effect of these materials. For example, 1 µg. or less of endotoxin was found sufficient to help establish a rapidly fatal septicemia with *Staphylococcus aureus*. Small amounts of endotoxin (1 µg. or less), administered alone, caused a marked but transient loss of weight.

"Vaccination with heat-killed Gram-negative bacilli or with killed BCG increased the resistance of NCS mice to the infection-enhancing effect of small amounts of endotoxin. This protective effect exhibited a certain degree of specificity for the bacterial strain from which the toxin used in the infection-enhancing test was derived.

"These various findings can be explained by assuming that the pathological effects of endotoxins involve at least two unrelated mechanisms; (a) a primary toxicity illustrated in this study by the loss of weight and enhancement of infection resulting from the injection of small doses of toxin; (b) an immunological reaction with lethal consequences which became manifest only in animals sensitized to the endotoxin by prior exposure to Gram-negative bacilli."

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—General; Antibiotics; other Therapeutic Substances; Disinfection.

CRONK, G. A. & WHEATLEY, W. B. **Penicillin: Oral or Intramuscular?** *Amer. J. Med. Sci.* 1960, Dec., v. 240, No. 6, 722–5, 1 fig.

In 2 cross-over experiments, each with 10 volunteers, and 1 experiment of Latin Square design with 15, the effects of oral phenethicillin were compared with those of intramuscular benzyl penicillin and of intramuscular phenethicillin, the single dose of each being 250 mgm. and the subjects all fasting. The penicillin content of the blood was determined $\frac{1}{4}$, $\frac{1}{2}$, 1, 2, 4 and in some tests 6 and 8 hours after the dose. The concentrations found are stated only as averages. There was no significant difference at any time interval between the concentrations resulting from the 3 forms of administration. The authors therefore argue that it should now rarely be necessary to give penicillin by injection, and they further commend the oral route as safer. [This argument disregards differences in antibacterial activity between benzyl penicillin and phenethicillin, almost all of which are in favour of the former.]

L. P. Garrod

MCCARTHY, C. G., WALLMARK, G. & FINLAND, M., with the technical assistance of Clare WILCOX & Joan H. YARROWS. **In vitro Activity of Various Penicillins.** *Amer. J. Med. Sci.* 1961, Feb., v. 241, No. 2, 143–59, 8 figs. [23 refs.]

This important paper reports tests of the *in vitro* activity against 552 strains of 20 species of bacteria of benzyl penicillin (G), phenoxymethyl penicillin (V), the 2 stereo-isomers of phenoxymethyl penicillin separately and in the proportions in which they usually exist in phenethicillin (D, L, and DL), phenylmercaptomethyl penicillin (PM) and synnematin B (SB). A plate dilution test with 2-fold differences was the principal method used; 2 different ways of inoculating the plates were compared and some tests were also done in liquid media. The results are given in both tabular and graphic form, the latter, as in numerous earlier papers from Finland's laboratory, showing the percentages of strain inhibited by different concentrations of each antibiotic.

SB was uniformly less active (usually much less) than the other penicillins against all organisms except in tests only briefly referred to against a few strains of *Salmonella* spp. and *Escherichia coli*. Against sensitive strains of *Staphylococcus aureus* the order of activity was V>G>L>DL>D with small differences; against penicillinase-forming strains D, L and DL were substantially more active than the others. PM and G were the most active against streptococci of all 3 species, and PM against pneumococci but with G ranking 4th [a finding contrary to observations by others]: all these differences were fairly small. They were greater in tests with 2 Gram-negative organisms, the gonococcus, against which G was the most active, with V and PM next, and D, DL and L showing progressively lower activity, and

Haemophilus influenzae, against which the order was the same, but with a wide difference between PM and V in favour of the former. Findings with smaller numbers of other Gram-negative species are reported briefly only in the text. The authors conclude that different penicillins possess varying degrees of activity against different bacterial species, and that these need to be taken into account as well as their pharmacological and other properties.

An addendum reports some findings with 2,6-dimethoxyphenyl penicillin (Celbenin: methicillin), which was available to the authors too late to include in the main series of tests. These findings confirm that methicillin is more active than G against penicillinase-forming staphylococci, but less active (usually much less) against all other species.

L. P. Garrod

i. TRINCA, J. C. & KEEN, T. E. B. **Penicillinase in Penicillin Reactions.** *Med. J. Australia.* 1960, Dec. 17, v. 2, No. 25, 973–6. [17 refs.]

ii. MATHEWS, A. G. & SEMPLE, N. M. **Laboratory Studies on the Purified Penicillinase of *Bacillus subtilis*.** *Med. J. Australia.* 1960, Dec. 17, v. 2, No. 25, 976–8.

i. This paper from the Commonwealth Serum Laboratories, Melbourne, reports the results of administering a purified penicillinase derived from *Bacillus subtilis* to 40 patients with penicillin reactions. Most of these were of urticarial type, a few taking other skin eruptive forms: none were of shock-like nature. The dose given intramuscularly varied from 350,000 to 800,000 units: 31 patients had a single dose, 7 had 2 doses, and 2 had 3. The results varied from almost immediate relief ("irritation had gone" within half an hour) to no effect: 20 patients (50%) were classed as improved. Better results followed early treatment than late: 7/9 were improved when penicillinase was given within 2 days of "their last known contact with penicillin", but only 8/22 when the interval was >2 weeks. [In 10 the interval was more than 2 months. Since the only effect of penicillinase is to destroy penicillin remaining in the body, it is difficult to see how any effect can be expected at this stage, unless on residues of benzathine penicillin, and it is not mentioned that this form of penicillin was given to any of the patients. Some were advised to restrict their milk intake, on the assumption that continued reactions might be due to penicillin from this source, but no attempt was made to prove this.] When repeated doses appear necessary they should be given at short intervals, since later a reaction may result from sensitization to penicillinase itself.

ii. The succeeding paper, by Matthews and Semple, describes the preparation and properties of the penicillinase used.

L. P. Garrod

GHOSH, D.; BORKAR, P. S.; SEN, G. **Studies on Penicillinase. I. A Modified Rapid Iodometric Method of Assay** [GHOSH & BORKAR]. *Hindustan Antibiotics Bull.* 1961, Feb., v. 3, No. 3, 85-91, 4 figs. [10 refs.] **II. Purification of Penicillinase** [GHOSH, SEN & BORKAR]. *Ibid.*, 92-6, 2 figs. [12 refs.]

BEVERIDGE, J. **Acute Chloramphenicol Poisoning in the New-Born Period.** *Med. J. Australia.* 1961, Jan. 21, v. 1, No. 3, 93-4.

An infant aged 17 days with an indurated and "suppurating" lesion of the skin of the thigh which started as a pustule was given 4 doses of 500 mgm. of chloramphenicol by injection at 12-hour intervals, after which he became pale, cold and cyanosed. Some improvement followed, but after admission to hospital and before any specific treatment was attempted, the state of vasomotor collapse appears to have been intensified and death followed in a few hours. The blood contained 160 μ gm./ml. of chloramphenicol. The author briefly reviews the literature of chloramphenicol poisoning in infants [this *Bulletin*, 1960, v. 35, 173, 596], and mentions that 3 similar but non-fatal cases had been seen at the Royal Hospital for Women, Sydney, in infants given chloramphenicol orally in a dose of 100 mgm. per kgm. daily: it is now considered that the dose should be 25 mgm. per kgm. [Writers on this subject do not explain how it ever came to be supposed that infants should be given much larger doses of chloramphenicol in relation to their weight than adults.]

L. P. Garrod

FIELDS, J. P. **Bulging Fontanel: a Complication of Tetracycline Therapy in Infants.** *J. Pediatrics.* St. Louis. 1961, Jan., v. 58, No. 1, 74-6.

"Tetracycline compounds can be a cause of increased intracranial pressure as manifested by bulging of the fontanel. This benign but alarming reaction disappears on withdrawal of the drug."

JACOBSON, E. D. & FALON, W. W. **Malabsorptive Effects of Neomycin in Commonly Used Doses.** *J. Amer. Med. Ass.* 1961, Jan. 21, v. 175, No. 3, 187-90, 4 figs.

These authors have previously found that large oral doses of neomycin interfere with intestinal absorption. They have now observed the effect in 10 patients of giving the more conventional dose of 4-6 gm. daily for 6-8 days. The plasma carotene level fell despite oral supplements of this substance: d-xylose urinary excretion after a loading dose of 25 gm. was diminished in 3 of the 4 subjects so tested, and faecal fat was increased in 1 subject in whom fat balance studies were made.

L. P. Garrod

CLUZEL, R., VERNER, M., VAURS, R. & CLUZEL-NIGAY, M. Comparaison du pouvoir bactéricide des associations d'antibiotiques au sein du groupe érythromycine - spiramycine - carbomycine - oléandomycine sur les staphylocoques pathogènes. [Comparison of the Bactericidal Power of Antibiotic Combinations within the Erythromycin-Spiramycin - Carbomycin - Oleandomycin Group on Pathogenic Staphylococci] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 875-82, 3 figs. [24 refs.]

These authors from Clermont-Ferrand used the Cellophane transfer method of Chabbert to examine the combined bactericidal action of pairs of the macrolide antibiotics named in the title. Tests of the 6 possible combinations were made with 12 strains of staphylococci, all being sensitive to these antibiotics, although not always to others. Combined action was found to be synergic in 38 of the total tests, indifferent in 30 and antagonistic in 4: examples of each type of result are furnished as illustrations. The combination erythromycin + oleandomycin was synergic against all 12 strains, whereas no other combination acted in this way against more than 6. [It is surprising that such closely related antibiotics should react mutually in these diverse ways. The synergy observed seems to call for verification by other methods.]

L. P. Garrod

PAPAVASSILIOU, J. **Biological Characteristics of Colicine X.** [Correspondence.] *Nature.* 1961, Apr. 1, v. 190, 110.

BRUCH, C. W. **Decontamination of Enclosed Spaces with Beta-Propiolactone Vapor.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 1-9. [15 refs.]

The authors describe the use of beta-propiolactone to decontaminate 3 areas: (1) an operating room, burn dressing room and premature nursery (together having a volume of 8,300 cu. ft.) in a hospital with a problem of staphylococcal sepsis; (2) a new maternity ward of 36 rooms and total volume of 89,000 cu. ft.; and (3) a new viral vaccine production building of total volume 52,700 cu. ft. The lactone was atomized in a special multiple spinning disc dispenser mounted on a push cart. In addition to the dispenser's own fan additional fans were used to distribute the vapour. Any openings through which vapour could escape were sealed with tape. The temperature was 75°-85°F. (24°-30°C.) throughout. When the relative humidity was below 85% this was raised by spraying water separately or by adding water to the lactone in the dispenser. After a contact time of 2-4 hours the vapour was removed either via the ventilating system of the building or by a charcoal filter. Samples of vapour taken immediately after exposure by workers wearing protective clothing showed lactone concentrations of 2.4-5.3 mgm. per litre.

The bacteriological efficiency of the process was tested by paper strips containing 10⁵ spores of *Bacillus subtilis*

var. *niger* or *B. stearothermophilus* and by swabbing small contiguous areas (4×4 ins.) of various surfaces before and after exposure. The strips were strategically placed in open drawers, under sinks and in similar places. Cultural results showed that the spore strips were sterilized except at one site. Here 2 out of 5 strips were sterile and the remainder had their count reduced to 0.1% of the original value. The results of the swabbing were less striking; about half the sites were sterilized. The remainder had their counts reduced by about 99%. The authors attribute these findings to recontamination after exposure. Slight damage to 2 painted and 1 plastic surface was done when the initial aerosol had impinged directly, but no damage was found in areas that had been exposed only to the vapour.

The authors consider this use of beta-propiolactone effective and suggest that it may be useful where large areas are contaminated with dangerous or exotic pathogens which have resisted other forms of treatment. The wider application of the method will depend on further definition of the toxicity and carcinogenicity of the agent used.

[These findings are in general agreement with those of HOFFMAN and WARSHOWSKY (this *Bulletin*, 1959, v. 34,

477) and SPINER and HOFFMAN (*ibid.*, 1960, v. 35, 1225).] J. C. Kelsey

LINCOLN, R. E. & ROTH, N. G. A Decontaminator-Washer-Dryer-Powderer for Surgical Gloves. *Applied Microbiol.* Baltimore. 1961, Jan., v. 9, No. 1, 81-4.

"A washer-dryer for surgical gloves is described. The machine is a modified household washer-dryer combination which performs a decontamination-wash, detergent-wash, two rinses, and a drying cycle. Gloves are removed at the completion of the described cycle, decontaminated, clean, dry, and powdered. Such gloves are satisfactory for immediate use for routine purposes or ready for wrapping and autoclaving for surgical use. It has given satisfactory operation in routine use in a 16 laboratory unit, using about 1,200 surgical gloves per week, for a period of 15 months. Use of the described machine resulted in a substantial saving of laboratory technician man hours and extended the life of the gloves as compared with processing by the hand operation in use at the testing laboratories."

BACTERIA

The order in this section is:—Cocci; *Donovania*; *Mycobacterium*; *Corynebacterium*; *Haemophilus*; *Pseudomonas*; *Pfeifferella*; Enteric Organisms; *Brucella*; *Pasteurella*; *Bacillus*; *Anaerobes*; *Spirochaetes*; *Erysipelothrix*; *Listeria*; Others.

THOMAS, Mair. The Sticky Film Method of Detecting Skin Staphylococci. *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council)*. 1961, Feb., v. 20, 37-40, 2 figs.

An improved method of skin sampling for staphylococci from contaminated surfaces is described. A strip about 1×3 inches of commercial adhesive tape is carried on a sterile glass slide, or on the manufacturer's prepared backing paper, one end is turned back to act as a tab.

In use the adhesive tape is stripped from the slide or backing paper, pressed to the surface (skin and other contaminated area) to be tested, and replaced on the slide or paper. In the laboratory the tape is pressed briefly to the surface of a culture plate and discarded. The slight sucking action of the sticky surface allows a map of the sampled area to be obtained.

The author discusses the brands of tape she found most satisfactory. She points out that this method gives a better qualitative result as well as being to some extent quantitative and samples are more easily sent by post.

M. Patricia Jevons

FERINA, F. & MELDOLESI, M. F. Alterazioni degli stafilococchi per sviluppo in terreni glicerinati 5%. I. Modificazioni della stabilità delle sospensioni batteriche. [Alterations of Staphylococci Grown in Media containing 5% Glycerol. I. Modification of the Stability of Suspensions] *Riv. Istituto Sieroterap. Ital.* 1960, Nov.-Dec., v. 35, No. 6, 613-21, 1 graph. [15 refs.] II. Modificazioni della agglutinabilità da agglutinine antistafilococciche. [II. Modification of Agglutinability by Immune Serum] *Ibid.*, 622-6, 1 graph.

The English summaries appended to the papers are as follows:—

I. "Some strains of *Staphylococcus pyogenes aureus*, when cultured in presence of 5% glycerol, show a different behavior, in comparison with the same strains grown on ordinary media, in the auto-agglutination test as various pH.

"The same strains show also a modified tendency to the agglutination by basic proteins (salmine) upon cultivation in presence of glycerol."

II. "Following previous investigations on the modification of *Staph. aureus* strains brought about by cultivation on nutrient agar supplemented with 5% glycerol, it has been shown that strains grown on such a medium are agglutinated to a lesser extent by anti-staphylococcus immune sera. Antigenic activity is not lost by cultivation in presence of glycerol.

"Modifications of the bacterial cells take place only during the growth phase."

CIUCĂ, M., POPOVICI, Marcella, NESTORESCU, N., ALEXENCO, Ecaterina & SOARE, Luiza. Die Lyso-genität im Zusammenhang mit anderen biologischen Eigenschaften der Staphylokokkenstämme. [Lyso-genicity and its Correlation to other Biological Properties of *Staphylococcus* Strains] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 3, 364-8. [13 refs.]

The English summary appended to the paper is as follows:—

"Two hundred and fifty nine staphylococcus strains of different provenience were tested using the classical 'in vitro' tests of pathogenicity. One hundred and seventy nine strains were listed as pathogenic and eighty as apathogenic. The latter strains proved to be phage resistant, non-lysogenic and apathogenic for mice. Out of the pathogenic strains 83.3 per cent were lysogenic. A direct correlation between lysogenicity, toxin production, and in vivo pathogenicity for mice could not be observed."

GARVIE, Ellen I., HIGGS, T. M. & NEAVE, F. K. Un-usual Varieties of *Staphylococcus aureus*. *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 255-9.

Variant strains of micrococci were isolated from swabs of cows' teats and nasal swabs of a laboratory worker and compared with known strains of *Staphylococcus aureus* and other micrococci. The strains differed from the type strain of *Staph. aureus* in the production and type of coagulase; failure to produce alpha toxin; inability to ferment mannitol and glucose anaerobically (2 strains). They could not be distinguished from coagulase-negative micrococci by biochemical tests.

The 5 strains fell into 2 groups, the 2 strains of one group produced bound coagulase and free coagulase in rabbit plasma. They produced acid and clot in litmus milk, fermented maltose and trehalose but failed to produce acetoin. Strains of the 2 groups differed in the opacity reached in shaken yeast glucose cultures incubated at 37°C. but an amino acid and peptide analysis obtained chromatographically suggested that strains of both groups should be regarded as *Staph. aureus*.

M. Patricia Jevons

SCARPA, B. Caratteri biochimici degli stafilococchi patogeni. [Biochemical Characters of Pathogenic *Staphylococci*] *Ann. Sclavo*. Siena. 1960, Sept.-Oct., v. 2, No. 5, 441-6, 1 fig. [10 refs.] English summary (7 lines).

The author studied 134 strains of staphylococci, 33 of which came from nasal swabs of healthy persons in normal environments, 63 from healthy persons in a hospital environment, and 38 from purulent lesions (furuncles, abscesses, infected operation wounds). The characteristics studied were mannitol fermentation on Chapman's salt medium, haemolysis on blood from rabbits, fowls, sheep, horse and man, presence of lipase, presence of coagulase sought on 4 different substrates, presence of fibrinolysin, of lecithinase and phosphatase, and of gelatinase.

Almost all the strains isolated from lesions were mannitol positive and α -haemolytic, although a fair proportion of staphylococci from other sources also gave positive results. β -haemolysis appeared in 80% of strains from lesions. The proportion of strains showing coagulase was not markedly greater than among those from other sources. On the whole, coagulases, proteases and α and β -haemolysins were frequent in strains from pathological material even though these might not have the full enzymatic complement. In effect only those staphylococci should be considered pathogenic which fulfil Koch's postulates, and which, having been isolated from a closed lesion, may have leucocidins and haemolysins, coagulase, fibrinolysins and hyaluronidase. Still *in vitro* tests cannot exactly match *in vivo* behaviour and insisting on this would exclude many staphylococci coming from closed pathological lesions.

We still lack a sure way of identifying pathogenic staphylococci; perhaps there is no such possibility either because pathogenicity depends on the susceptibility and defence powers of the host, or because there may be infinite gradations between saprophytism and parasitism.

E. Agius

RICHO, R. Sur la resistance à la chaleur des hemolysines staphylococciques. [The Heat Resistance of *Staphylococcal Haemolysins*] *Ann. Sclavo*. Siena. 1960, Sept.-Oct., v. 2, No. 5, 447-53. [15 refs.]

An investigation of staphylococci associated with a food-poisoning incident through meat stimulated the author to study the heat resistance of staphylococcal haemolysins on which the views of other workers were found to have been discordant. 26 toxins with pH ranging from 7.4 to 8.4 were studied. 12 of these contained only α -haemolysin and 14 contained both α and β . All the α -lysins retained a high haemolytic power for rabbit cells after heating at 50°C. for 30 minutes. After heating at 60° and 70° only 2 toxins showed a considerable haemolytic activity. After heating at 80°, 7 toxins and after 90°, 6 toxins still showed weak haemolytic power. After heating at 100° those 2 which had shown resistance at 60° still retained some haemolytic power which they only lost when heated at 110°.

The toxins containing α and β -lysins lost their α -haemolytic power after 60° but retained some β -potency, which later resisted even 70°. After heating at 100° only 2 toxins retained lytic power for sheep cells.

It appears that under the conditions indicated (within the pH shown) 60° appeared most active for α -lysin and 100° for the β -lysin. When using heat, it appears necessary to confirm in each case that a toxin has in fact been inactivated.

E. Agius

ALAMI, S. Y. & KELLY, Florene C. **Influence of Coagulases and Route of Injection on Staphylococcal Virulence in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 589-91, 1 fig.

The effect of free and bound coagulase on the virulence of staphylococci was compared by injection of strains into mice by various routes. 12 strains were chosen for study representing coagulase-positive and coagulase-negative strains as well as variants selected from these strains which lacked either free or bound coagulase. They were divided into 4 groups:—

Group I, 4 strains producing free and bound coagulase.

Group II, 3 stable strains producing free but no bound coagulase.

Group III, 3 strains producing bound but no free coagulase.

Group IV, 2 strains producing no free or bound coagulase (variants of 2 strains in Group I).

The LD₅₀ of all strains by intravenous and intraperitoneal routes was determined by injecting washed cells from 24-hour broth cultures in various dilutions into batches of mice. Mice were also injected intraperitoneally with cells suspended in 5% hog gastric mucin. They were observed for 14 days and organs were examined culturally and microscopically.

The LD₅₀ was not influenced by the presence of free or bound coagulase by whichever route the organisms were injected. The 3 strains in Group II showed enhanced virulence when injected intraperitoneally in mucin regardless of the coagulase titre but the virulence of the other strains was not enhanced.

M. Patricia Jevons

GRÜN, L. **Über neue Staphylokokken-Antigene. [On New Staphylococcal Antigens]** *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 2, 210-15. [14 refs.]

In a study of 3 strains of *Staph. aureus* 2 new type antigens have been discovered, and are now named 'o' and 'p'; the 'o' antigen is heat-labile, the 'p' heat-stable. They differ from the 'm' and 'n' antigens recently described by HAUKENES and OEDING (*Acta Path. et Microb. Scandinavica*, 1960, v. 49, 237).

R. E. O. Williams

COLLINS, Anne M., DUNCAN, I. B. R., NEELIN, Elisabeth M., ZNAMIROWSKI, R. & ROY, T. E. **Some Serological Properties of Substances extracted from Staphylococci and a Hemolytic Streptococcus.** *Canadian J. Microbiol.* Ottawa, 1960, Dec., v. 6, No. 6, 661-72. [11 refs.]

The authors set out to find a method of detecting antibodies directed against cellular constituents of staphylococci in animal sera. A coagulase positive staphylococcus, a coagulase negative staphylococcus and a Type 12 Group A streptococcus were chosen for study and animals were immunized with 3 vaccines; an alcohol killed preparation; a "polysaccharide" extract prepared by phenol extraction and alcohol precipitation, and the same extract adsorbed on to Group O erythrocytes. Sera

thus prepared were tested by agglutination, haemagglutination and latex agglutination techniques.

The antisera produced by injection of extracts alone were poorly antigenic. Antisera produced by whole bacteria and extract-sensitized erythrocytes agglutinated sensitized cells to titres between 160 and 640. These reactions, however, were not specific. Latex agglutination tests in buffer at pH 8.2 gave similar cross reactions which were more marked in sera produced by extract-sensitized erythrocytes than whole organisms. Agglutination tests were unsatisfactory owing to spontaneous agglutination of the coagulase negative staphylococcus and the streptococcus.

Mirror absorption tests of sera prepared by extract-sensitized erythrocytes absorbed by sensitized cells failed to give clear-cut evidence of species specific antigens and chemical analysis of the "polysaccharide" extracts showed them to be of great complexity.

M. Patricia Jevons

STAMP (Lord). **Antibacterial Immunity to Staphylococcus pyogenes.** *Brit. J. Exper. Path.* 1961, Feb., v. 42, No. 1, 30-37, 1 fig. [22 refs.]

On the grounds that nearly all strains of staphylococcus which have a relatively high virulence for rabbits are strongly α -toxigenic and that the production of fresh toxin *in vivo* in large amounts is liable to overwhelm antibacterial defence mechanisms, the author chose strain 13 (phage types I-III), which met the requirements of weak α -toxin production and relatively high virulence for rabbits, for vaccine preparation. The vaccines, which were given to rabbits subcutaneously, consisted of a soluble fraction obtained from washed cells by ultrasonic disruption (and in one experiment by shaking with glass beads). The animals were satisfactorily protected when challenged, 3-6 weeks after immunization, with a 24-hour culture of the same strain. In all the experiments the sera of the immunized animals were tested for anti- α lysin and were consistently found to be negative at a level of 0.1 i.u. and above. These results support Forssman's contention that under certain conditions staphylococcal vaccines are capable of inducing specific immunity in rabbits in the absence of the production of circulating antitoxin. The author (in experiments to be reported later) has confirmed the demonstration of capsules in young cultures of normal coagulase-positive strains of staphylococcus, and suggests that a study of capsule swelling antibody in relation to immunity might be a fruitful line of investigation.

D. A. Cannon

JEVONS, M. Patricia., ROLINSON, G. N., & KNOX, R. **"Celbenin"-Resistant Staphylococci.** [Correspondence.] *Brit. Med. J.* 1961, Jan. 14, 124-6.

During October and November 1960, Jevons received 5,440 strains of *Staphylococcus aureus* at the Staphylococcus Reference Laboratory, Colindale, and tested them for sensitivity to Celbenin (BRL 1241) [this *Bulletin*, 1961, v. 36, 173, 174, 175]. 3 cultures were found to be resistant; all were derived from 1 hospital and belonged to phage type 7/47/53/54/75/77, 2 were from patients

and 1 from a nurse with a skin lesion. 1 of the patients had attended the hospital in July and a culture of staphylococci isolated at that time was still available; it also proved to be resistant to Celbenin and of the same phage type. No direct connexion between this patient and the later infections was discovered but in view of the identity of types it seems likely that they were all part of 1 episode. Celbenin treatment was not employed for any of the patients yielding the resistant strains, and had only been employed for 1 patient in the hospital, infected with a type 80/81 strain.

Rolinson confirms the laboratory results reported by Jevons and has found that the resistant cultures consist of a mixture of very small numbers (e.g. 1 in 10⁷) of cells resistant to high concentrations of Celbenin with a large number of cells of the same phage type with substantially normal sensitivity.

Knox also reports the finding that the resistant cultures have cells of widely differing sensitivity. In contrast to a laboratory-trained strain resistant to 500 µgm./ml. Celbenin, the naturally occurring resistant strains have a normal growth rate.

R. E. O. Williams

KÖHLER, W. Die Typisierung hämolysierender Streptokokken der Gruppe A. I. Mitteilung: Methoden der Typisierung und die Herstellung agglutininierender Seren. [Typing of Haemolytic Streptococci of Group A. I. Methods of Typing and the Preparation of Agglutinating Sera] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Nov., v. 120, No. 4, 253-78. [39 refs.]

This paper presents a brief but competent review of our present ideas on the type antigens of group A streptococci and of the methods of type identification based on the T antigen. There is a useful list of the standard type strains employed and some documentation of the cross-reactions between types recorded in the literature.

R. E. O. Williams

KÖHLER, W. & HEINRICH, H. Die Typisierung hämolysierender Streptokokken der Gruppe A. II. Mitteilung: Die Verbreitung der Streptokokkentypen im Bezirk Schwerin. [Typing of Haemolytic Streptococci, Group A. II. Distribution of Different Types of Streptococci in Schwerin Area] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1961, Feb., v. 121, No. 1, 56-74. [39 refs.]

Between January and September 1960 a total of 520 strains of haemolytic streptococci isolated from 466 patients in the Schwerin district of Germany (Democratic Republic) were examined. The results are presented in detail. Type identification was based solely on the T antigens. Type 6 was the commonest type (15.4% of patients) and type 12 the next (4.6%). 14% of strains showed various mixed reactions. 21% were untypable although group A. Several type distributions from the published literature are summarized [but not the 4-year Public Health Laboratory Service Survey in England and Wales, this *Bulletin*, 1958, v. 33, 70].

R. E. O. Williams

WILEY, G. G. & WILSON, A. T. The Occurrence of Two M Antigens in Certain Group A Streptococci Related to Type 14. *J. Exper. Med.* 1961, Feb. 1, v. 113, No. 2, 451-65. [25 refs.]

A strain of Type 14 Group A streptococcus which had previously given a good long-chain reaction in the presence of homologous anti-M serum was found, on repetition of the test, to consist of short- as well as long-chain microcolonies. 12 colonies of a subculture of the strain were further investigated by the long-chain reaction and by testing acid extracts of subcultures for precipitation with anti-M serum. 7 of the cultures reacted strongly and 2 weakly with Type 14 anti-M serum and grew as a mixture of long- and short-chained microcolonies and 3 cultures failed to give a precipitation reaction with Type 14 serum and grew only in the short-chain form.

Mouse virulence and bactericidal tests of a representative M positive colony (colony 3) and the presumed M negative colony (colony 7) were carried out. [There is no mention that these colonies had the same Type antigen as the parent strain.]. These tests showed that colony 3 was highly virulent and grew in human blood while colony 7 was moderately virulent and not so readily phagocytosed as typical M-negative strains. The resistance to ingestion of colony 7 was increased by mouse passage but an M antigen was not demonstrated by testing with the available M antisera.

Results of testing antisera prepared against colony 3 and colony 7 suggested that colony 3 carried 2 precipitating antigens, one of these only being carried by colony 7. Bactericidal tests confirmed this and demonstrated that the antigen carried only by colony 3 was the currently recognized Type 14 M antigen. The other antigen shared by both subcultures possessed the properties of an M antigen in that it was extractable by hot acid, trypsin-sensitive, located on the cell wall and inhibited the growth of the homologous strain in the bactericidal test. The New M antigen was called Type 51 antigen and strains possessing both antigens (e.g. colony 3) were called Type 14-51.

Of the 42 strains of Type 14 and strains thought to be related, which were examined, 37 possessed both antigens, 4 had only Type 51 antigen and 1 strain carried only Type 14 antigen. [It would be interesting to know if, when the 51 antigen occurred alone, it was weak, detectable only in a concentrated M extract, or if it could be demonstrated in an ordinary crude acid extract.]

This is the first report of 2 M antigens possessed by a single strain of Group A streptococcus and the authors point out that failure of a subculture to produce the M antigen of the parent strain need not invariably mean that no M antigen is produced.

M. Patricia Jevons

GABBRIELLI, G., SALETTI, M. & PIAZZI, S. E. La tossina streptococcica. I. Titolazione del potere letale sull'embrione di pollo. [Streptococcal Toxin. I. Titration of its Lethal Power on Chick Embryos] *Ann. Sclavo.* Siena. 1960, Sept.-Oct., v. 2, No. 5, 535-47, 2 graphs. [15 refs.] English summary (6 lines).

The authors used a toxin from a group A *Streptococcus pyogenes* grown on a horse-meat tryptic digest

medium, which was first lyophilized and then dissolved in small volumes of distilled water to produce a highly concentrated preparation. They concluded that while rats were markedly resistant, white mice were relatively susceptible and rabbits were the animals of choice. Still, the doses of filtrate producing death were enormous compared with those necessary with toxins such as those of tetanus, diphtheria, and even of staphylococci. Economic and practical considerations are against the extensive use of rabbits in the numbers which are often necessary. These reasons prompted the authors to investigate the use of chick embryos.

Using the well-known techniques described by BEVERIDGE and BURNET [this *Bulletin*, 1947, v. 22, 89], the authors inoculated 0.1 ml. volumes of various dilutions of the same toxin previously used into the yolk sac. The time to death was taken, on the basis of numerous observations, as 48 hours. By testing on 360 embryos, the determination of the LD100 was found to be 1/600 ml., in contrast with 5 ml. for white mice and 6 ml. for rabbits. On the basis of 4 tests with 10 embryos at a time, the LD50 was found to be 1/1750 ml. This shows chick embryos to be by far the most sensitive. By its convenience, ease and the reproducibility of results this test seems to be clearly preferable to tests in which other animals are used.

E. Agius

ROTTA, J. & ZEMAN, K. Clearance beta hemolytických streptokoků značených P³² z krve a rozmístění v orgánech retikuloendoteliálního systému myši po experimentální infekci. [Clearance of Beta-Haemolytic Streptococci Labelled with ³²P from the Blood and their Distribution in Organs of the Reticuloendothelial System of the Mouse after Experimental Infection] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 8, 509-16, 5 graphs. [17 refs.] English summary (7 lines).

Streptococci were labelled with ³²P by cultivation in a medium containing labelled disodium phosphate and were injected into mice intravenously; their subsequent fate in the blood was investigated by determination of the radioactivity of blood samples taken at intervals after infection, and of the organs removed at autopsy. The organisms were found to disappear from the blood exponentially, and only 10% were still present after 8 minutes; after 16 minutes 54.2% of the injected radioactivity was found in the liver, 0.65% in the spleen, 0.34% in the kidneys and 5.2% in the lungs. After intraperitoneal injection of labelled organisms radioactivity was again found in the liver, but somewhat higher proportions were found in the spleen (14.6%), kidneys (10.5%) and lungs (7.4%).

D. J. Bauer

HALBERT, S. P., BIRCHER, R. & DAHLE, E. The Analysis of Streptococcal Infections. V. Cardiotoxicity of Streptolysin O for Rabbits *in vivo*. *J. Exper. Med.* 1961, Apr. 1, v. 113, No. 4, 759-84, 8 text figs. & 1 coloured fig. on pl. [44 refs.]

LI, Yu-Teh. & SHETLAR, M. R. Utilization of Serum α_1 -Globulin and Glycoprotein by *Diplococcus pneumoniae*. *Proc. Soc. Exper. Biol. & Med.* 1961, Feb., v. 106, No. 2, 398-400, 1 fig.

"When serum samples were incubated with a rapidly growing strain of *Diplococcus pneumoniae*, striking decreases of serum glycoprotein and consistent decreases of protein resulted. Paper electro-phoretic studies indicated that these changes were largely restricted to the α_1 -globulin fraction. It would appear that this strain of *Diplococcus pneumoniae* preferentially uses glycoproteins found in the α_1 -globulin fraction."

KERREST, J. Procédé de fermeture des tubes de culture pour *Mycobacterium tuberculosis*, permettant d'éviter les contaminations par les champignons en régions tropicales. [Sealing of Culture Tubes for *Mycobacterium tuberculosis* which avoids Contamination by Fungi in Tropical Regions] *Bull. Soc. Path. Exot.* 1960, Sept.-Oct., v. 53, No. 5, 785-6.

In the tropics there is a high contamination rate of cultures for tubercle bacilli by moulds, especially when cotton-wool plugs and rubber caps are used. The author claims to have overcome this problem without interfering with the aeration of the culture, by removing the cotton-wool plug after 2 days' incubation and replacing it with aluminium foil. The foil, which is 4 cm. square, is sterilized in the hot-air oven, placed over the mouth of the tube and folded over the sides; it is held in place with adhesive tape. He considers the method superior to screw-cap bottles.

S. R. M. Bushby

CASAS-CAMPILLO, C. & BOJALIL, L. F. The *in vitro* Effect of 21-21-Dimethoxy Progesterone on Acid-Fast Microorganisms. *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 272-5, 1 fig. [Refs. in footnotes.]

"21-21-Dimethoxy progesterone (DMP) inhibited to a significant extent the growth of 43 different strains of mycobacteria at concentrations from 1 to 100 γ per ml. Photochromogens, non-photochromogens, scotochromogens, and avian mycobacteria were more susceptible to the steroid than were fast-growing and human strains. Viomycin-, isoniazid-, or streptomycin-resistant strains of *M. tuberculosis* were inhibited by the steroid at concentrations from 25 to 50 γ per ml. Some degree of synergic action was observed with mixtures of DMP and isoniazid in *M. smegmatis* 607. *Nocardia asteroides* and *N. brasiliensis* were also inhibited by 1 to 10 γ of DMP per ml. Strains of *N. asteroides* resistant to 4,4'-diaminodiphenyl-sulfone showed susceptibility to 1 γ of the steroid per ml."

FODOR, T. & KERTAY, N. Die Wirkung von Dextran auf die experimentelle Meerschweinchen-Tuberkulose. [The Influence of Dextran on the Experimental Tuberculosis of Guinea-pigs] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 2, 249-52.

The English summary appended to the paper is as follows:—

"The addition of dextran increased the activity of tubercle bacilli in experimental guinea pig infections. The same amount of tubercle bacteria produced considerably severer tuberculosis when injected intramuscularly together with dextran than without it. This fact may be useful for the bacteriological routine diagnosis of tuberculosis."

UYEDA, S., UESAKA, I. & DOHI, K. Modification de la virulence du bacille tuberculeux chez la souris par l'enrobage dans l'huile de paraffine. [Modification of the Virulence of Tubercle Bacilli for the Mouse by coating with Liquid Paraffin] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8-9, 1703-7, 4 figs.

The tubercle bacilli were grown in glycerol broth, dried with filter paper and suspended in liquid paraffin or normal saline. The bacilli were then inoculated intraperitoneally into mice.

Judged by survival time, the virulence of the H37Rv and Ravenel bovine strain was decreased by the coating with oil, for with the Ravenel strain all the mice infected with the saline suspension were dead within 15 days whereas only 50% of those infected with the oily suspension were dead in 42 days. With less virulent strains, however, the oily strains were the more virulent, for the oily suspension of BCG killed all the animals in 25 days whilst the saline suspension killed none, and an avian strain behaved similarly.

Post-mortem examinations of the mice inoculated with the oily suspensions showed adhesions of the abdominal organs, and impression smears of cut-surfaces of the viscera showed the bacilli to be well dispersed extracellularly, and to be adherent to droplets of oil.

S. R. M. Bushby

VANDIVIERE, H. M., VANDIVIERE, Margaret R. & SEIBERT, Florence B. Comparison between Purified Individual Tuberculoproteins and the International Standard Tuberculin. *J. Infect. Dis.* 1961, Jan.-Feb., v. 108, No. 1, 45-52, 1 fig. [10 refs.]

"A trifold method of measuring tuberculin reactions is described. It appears to be more sensitive for quantitative assessment than other methods in use and permits a more critical and valid evaluation of comparisons.

"Several proteins prepared from unheated tuberculin filtrates and 1 isolated from bacillary bodies (designated as A, B, C and bacillary protein) were compared at various dose levels with comparable PPD-S as skin test antigens in known tuberculous patients and in people vaccinated with a human strain vaccine (R₁R_v) or a bovine strain vaccine (BCG), as well as in nontuberculous but naturally sensitized individuals.

"The C protein fraction proved to be considerably less sensitive and possibly less specific than the standard PPD-S in all subjects, indicating that its presence in PPD may dilute the strength.

"The B protein appeared to be more sensitive and possibly more specific as a skin test antigen than PPD-S."

TAKAHASHI, Y. & YAMAMOTO, K. Constituants du bacille tuberculeux déterminant l'allergie et l'immunité dans la tuberculose. [Constituents of the Tubercle Bacillus in determining Allergy and Immunity in Tuberculosis] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1694-7, 2 figs.

Groups of 4-8 guineapigs were vaccinated with 1.0 mgm. tubercle bacilli (BCG), treated by immersion in acetone (BA), 0.72 mgm. of the bacilli after successive extraction with acetone, methanol and chloroform and hydrolysed with 1% hydrochloric acid in alcohol (RHA), and also with 0.89 mgm. of similarly extracted bacilli but hydrolysed with 2% hydrochloric acid (RHD); these doses were based on equivalent nitrogen contents. The antigens were injected suspended in an aqueous medium or in liquid paraffin plus tubercle bacilli wax. A second injection of each antigen, but at 10 times the first dose, was given 3 weeks later. The animals were tested at weekly intervals with 1:100 tuberculin and 6 weeks after the first injection they were challenged with virulent tubercle bacilli. A control group of guineapigs were vaccinated with BCG. Post-mortem examinations were made on all the animals 6 weeks after the challenge.

The results showed that neither RHA nor RHD afforded protection when injected in saline but when given in the oil and wax they gave protection to a similar degree to that given by BA and BCG, although the sensitivity to tuberculin was very much less, indicating that antigens can be prepared that can stimulate a high degree of protection without inducing a high state of sensitivity. The wax is considered to act as an adjuvant by stimulating an inflammatory reaction, and the results to indicate that conjugation between lipids and the proteins and polysaccharides is not essential for the stimulation of immunity.

S. R. M. Bushby

TAKAHASHI, Y., KUWAJIMA, T. & YAMAMOTO, K. Étude sur l'immunisation antituberculeuse par les constituants du bacille tuberculeux. [Study of Antituberculous Immunization by the Constituents of the Tubercle Bacillus] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1697-9, 2 figs.

Groups of 6-7 guineapigs were vaccinated with 4 fractions from tubercle bacilli:—polysaccharide extracted with urea containing 0.72% N; phosphatide extracted with methanol and containing 0.35% N and 2.8% P; wax extracted with chloroform containing 0.02% N; and PPD containing 13.6% N. They were injected intramuscularly suspended in mineral oil containing 10% of the detergent, arlacel; the dose was 1 mgm. for each fraction, the polysaccharide being given alone and the others in combination, and they were given as a single injection and also as 3 injections at 8-day intervals. The

animals were tested at intervals with 1:100 tuberculin and challenged with virulent tubercle bacilli 6 weeks after the first vaccination; post-mortem examinations were made 6 weeks after the challenge.

All the antigens gave some protection but it was least with the polysaccharide alone, and the protection increased progressively as the antigens were added to the polysaccharide in the order, PPD, phosphatide and wax. The degree of sensitization to tuberculin paralleled the degree of protection, the animals given the polysaccharide reacting least and those given the 4 antigens reacting most strongly. However, although the protection afforded by the polysaccharide was low and did not differ significantly from that given by an antigen consisting of 1 mgm. of killed tubercle bacilli, the latter produced a much greater degree of tuberculin-sensitivity indicating that allergy is not implicated in immunity.

S. R. M. Bushby

ARIMA, J. & YAMAMOTO, K. La culture des tissus comme moyen d'étude de l'immunité antituberculeuse. [Tissue Cultures as a means of Studying Antituberculous Immunity] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1700-703.

By using their spleen culture technique [this *Bulletin*, 1960, v. 35, 181] the authors show that the tubercle bacilli in the cultures from immunized guineapigs, inoculated intravenously, show little or no increase during 3 days' incubation, whereas in similar spleen cultures of non-immune guineapigs, the bacilli increase 3-7.7 times.

Using this method, they show that if vaccinated animals are desensitized by repeated doses of tuberculin, given during the period of development of immunity, growth in spleen culture is still inhibited, whereas if the animals are treated with prednisolone, they develop sensitivity to tuberculin but apparently no immunity, for the bacilli increase 5.7-10 times in the culture.

The authors point out that it is interesting to note that in these cultures the bacilli are mainly extracellular and thus differ from cultures made with peritoneal exudative cells.

S. R. M. Bushby

REES, R. J. W. & GARBUTT, Elizabeth W. Development of Immunity to Tuberculosis in Adult Mice injected with Tubercle Bacilli during Foetal Life. *Immunology*. Oxford. 1961, Jan., v. 4, No. 1, 88-93, 1 fig. [17 refs.]

On the 15th, 16th and 17th day of foetal life, the uterus of pregnant mice was exposed and the embryos were injected with 5×10^5 viable units of BCG suspended in 0.01 ml. saline; the maternal mortality was low but only about 50% of the litters were viable. Histological examination at birth showed acid-fast bacilli in the liver, spleen and lungs, with many of the bacilli being intracellular, and when 40-50 days old, examination of some of the mice showed a few bacilli still present within foci of round cells in these organs.

When 5-6 months old, 8 vaccinated mice were revaccinated with 8×10^7 viable units of BCG, and although

the mice were obviously ill on the following day, whereas normal mice vaccinated at the same time were unaffected, they recovered eventually. When the mice were killed 36 days later, histological examination revealed no differences between the 2 groups and the total counts of the bacilli in the spleens showed that the BCG had increased 4 times more in the control unvaccinated animals than in the mice vaccinated *in utero*. In another experiment in which the *in utero* vaccine consisted of killed bacilli, the viable BCG used in the challenge again multiplied more in the normal mice. In the final experiments, 20 mice vaccinated *in utero* with living BCG were challenged 5-6 weeks after birth with H37Rv, and whereas 6 of the animals survived for 44 days, giving a median survival time of 28 days, unvaccinated mice infected at the same time were all dead by the 31st day, giving a median survival time of 21 days. As in the first experiment, the vaccinated mice were ill on the day after challenge, and the authors attribute this to tuberculin shock.

The authors interpret these results as showing that exposures of mice *in utero* to BCG induces states of immunity and hypersensitivity to tuberculin rather than tolerance. As these results may, however, be caused by the antigens of the tubercle bacilli being released too slowly from the intact bacilli, owing to the short foetal life, the authors suggest that tolerance might develop if disrupted bacilli or fractions were used.

S. R. M. Bushby

TACQUET, A. & TISON, F. Mesure de la sensibilité des Mycobactéries tuberculeuses et atypiques aux associations d'antibiotiques. Technique nouvelle. [Estimation of the Sensitivity of *Mycobacterium tuberculosis* and the atypical bacilli to Antibiotics. A New Method] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1551-5.

In this method 1 ml. of a solution of the antibiotic is placed at the bottom of a Löwenstein-Jensen slope and the tube is kept vertical during the process of inoculation and incubation. The method is only applicable to the soluble drugs, and if a suitable concentration of the drug is used the height of the area of inhibited growth is a measure of the sensitivity of the bacilli, e.g. 0.5 µgm. isoniazid per ml. inhibits a sensitive strain for a distance of 36 mm. and a partially resistant strain for 17 mm., and 5 µgm. streptomycin per ml. gives somewhat similar zones.

The method is claimed to be of particular value as a screening test for the atypical acid-fast bacilli because they usually require testing against a wide range of drugs. [The method would seem to be less convenient than the disc method already recommended by several authors.]

S. R. M. Bushby

TSUKAMURA, M. Further Mutational Studies on the Isoniazid Resistance of *Mycobacterium tuberculosis*. *Japanese J. Microbiol.* 1960, Apr., v. 4, No. 2, 115-22.

"Increasing level of isoniazid resistance in *Mycobacterium tuberculosis* var. *hominis*, strain H37Rv, occurred

in a discontinuous manner, and about six types of the stable population structure, or mode of resistance, could be noted in clones obtained by different steps of selection. It was shown that there are about (at least) six phenotypes of the isoniazid resistance in this organism. It is conceivable that the isoniazid resistance of the organism is controlled by a few genes, and mutations of the genes occur independently."

BAYLET, R., CAMAIN, R. & BASSET, A. Tentative de culture de bacilles de Hansen sur cellules de rein de singe. [Attempts to Cultivate Hansen Bacillus in Monkey Kidney Cells] *Bull. Soc. Path. Exot.* 1960, Sept.-Oct., v. 53, No. 5, 836-41, 2 figs. on pl.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 803.]

TSUKAMURA, M. & ABO, T. *In vitro* and *in vivo* Anti-tuberculous Action of Neocidin, a New Antibiotic produced by a Number of the *Bacillus subtilis* Group. *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 381-5, 2 figs.

Neocidin is an antibacterial substance extracted from the pellicle growth of a strain of *Bacillus subtilis*, 0-25, and 1 unit of the antibiotic is that amount which inhibits the growth of *Mycobacterium avium* in 1 ml. of Sauton medium. In Dubos medium 32 units per ml. inhibited the growth of H37Rv but 1,600 units per ml. were necessary to inhibit the growth of this strain in Ogawa egg medium. Judged by the decrease in the number of viable tubercle bacilli in mice infected subcutaneously, 1,000 units of Neocidin per day given subcutaneously has some *in vivo* activity; the number of bacilli were reduced 10-fold after 6 weeks' treatment as compared with a 100-fold decrease by 2 mgm. streptomycin per day.

After 5 passages the minimum inhibitory concentration of Neocidin for *Myco. avium* increased in a step-wise manner from 0.5 unit per ml. to 256 units per ml. but the resistant variant showed no significant change in sensitivity to streptomycin, kanamycin, viomycin, isoniazid, PAS, sulphathiazole, sulphisoxazole, or Tibione [thiacetazone]. Variants of *Myco. avium* resistant to isoniazid, streptomycin, kanamycin or viomycin were still sensitive to Neocidin.

S. R. M. Bushby

ZITRIN, Charlotte M. & LINCOLN, Edith M. Initial Tuberculous Infection due to Drug-Resistant Organisms. With a Review of the World Literature on Initial Infection due to Isoniazid-Resistant Tubercle Bacilli. *J. Pediatrics*. St. Louis. 1961, Feb., v. 58, No. 2, 219-25. [20 refs.]

This report was produced by the Committee of the Section on Diseases of the Chest of the American Academy of Pediatrics which conducted a survey among its members, representing 33 pediatric clinics, to determine the incidence of isoniazid-resistant tubercle bacilli in

children with primary tuberculosis. Although 31 of the clinics made routine gastric cultures, only 7 regularly made sensitivity tests. A total of 2,500 patients were examined at these 7 clinics since the introduction of streptomycin and 325 yielded positive pre-treatment cultures, of which 11 were resistant to streptomycin, 3 being resistant to 2-10 μ gm. per ml. and 8 to 100-300 μ gm. per ml. Since isoniazid was introduced, 1,800 patients have been examined and 235 gave positive cultures, of which 4 were resistant to 1-5 μ gm. isoniazid per ml. and 3 to 10-50 μ gm. per ml., 5 of these strains were resistant to both drugs. Catalase tests were done on only 3 of the isoniazid-resistant strains (resistant to 1, 5 and 50 μ gm. per ml.) but all were positive. Short case histories are given of the 7 isoniazid-resistant cases and all but 1 of the patients recovered.

In addition to these cases, 2 patients with streptomycin-resistant bacilli were reported from the 21 clinics that did not do regular sensitivity testing. The report also reviews the literature on tuberculous infections caused by isoniazid-resistant strains.

S. R. M. Bushby

CSILLAG, Anna. Morphological and Biochemical Features of 'Atypical' Mycobacteria. *J. General Microbiol.* 1961, Feb., v. 24, No. 2, 261-72. [25 refs.]

Of these 42 strains, 16 were originally classified as Runyon Group I, 4 as Group II, 19 as Group III and 3 as Group IV; 13 of the strains were from patients in Britain and 29 were from America. In this study the strains were observed for morphological and cultural characteristics when growing in Kirchner, Löwenstein-Jensen and 7H-10 media, for ability to grow on nutrient and blood agar and gelatin, for rate and temperature range of growth, pigmentation, catalase activity, production of niacin, and sensitivity to isoniazid, PAS, streptomycin, thiacetazone, thioamide and cycloserine.

All the strains were niacin-negative and resistant to isoniazid and PAS; they were all strongly catalase-positive except for some of the Group III strains which were less strongly positive. All the strains grew at 22°C. and only those of Group IV grew on gelatin in 6 weeks and on nutrient agar within 3 days. The strains of Groups II and III showed no tendency to cord, but 15 of those of Group I grew in loose cords and all those of Group IV grew in tight cords. The strains of Group I grew as rough colonies, those of Group II as smooth colonies, those of Group III as variable colonies, and those of Group IV in a manner similar to H37Rv. The bacilli of Group I were long and beaded but the others were variable. Many of the bacilli of Group III were not acid fast; the bacilli of Groups I and II were positive with the periodic-acid-Schiff reagent, but those of III and IV, like H37Rv, were negative.

The niacin test was considered the most useful test for distinguishing those bacilli from human tubercle bacilli. The production of pigment was valuable for distinguishing Groups I, II and III and ability to grow on blood and nutrient agar for identifying Group IV.

S. R. M. Bushby

JOIRIS, E. Méthode rapide de coloration différentielle du bacille diphtérique. [Rapid Method for Differential Staining of Diphtheria Bacilli] C.R. Soc. Biol. 1960, v. 154, No. 7, 1496-8.

The author, from the University of Liège, describes a differential staining method for diphtheria bacilli in which the contrast between them and other bacteria is particularly striking. It is based on the fact that methylene blue in acetic acid stains the metachromatic granules intensely, while the cytoplasm is weakly stained. When the preparation is then counterstained with safranin, the cytoplasm is stained pink and the staining of the granules is so accentuated as to appear black: this produces a striking contrast between the granules and the cytoplasm.

The fixed smear is first stained for 10 to 20 seconds with Solution A, washed, drained and then stained for 1 minute with Solution B, when it is washed and blotted dry. Solution A consists of:

Methylene blue, extra (Merck)	0.3 gm.
95% ethyl alcohol	15 ml.
Glacial acetic acid	1 ml.
Distilled water	120 ml.

The acid is added last.

Solution B consists of:

Safranin O (National Aniline Division TDC 87%) ...	0.08 gm.
Distilled water	100 ml.

The author has compared the method with the usual technique in which an alcoholic solution of methylene blue is used. 100 preparations were examined and these included *gravis* and *mitis* types of *Corynebacterium diphtheriae*, diphtheroids, various other Gram-positive and Gram-negative organisms and mixed suspensions of pharyngeal cultures and pure *C. diphtheriae*. There was complete concordance in the results of the two methods in the case of diphtheria bacilli. Organisms other than corynebacteria, despite their contact with methylene blue, stained uniformly pink. In mixed cultures the method was therefore particularly useful, as the metachromatic granules of diphtheria bacilli stood out very clearly. Experiments in extending the period of staining up to 120 seconds for the methylene blue and 3 minutes for the safranin showed that the only difference was accentuation of the staining. The morphology of the diphtheria bacilli is completely preserved in this method.

H. J. O'D. Burke-Gaffney

CIUCĂ, M., CALALB, G., SARAGEA, Alice & MAXIMESCO, Paula. Particularités des "éco-systèmes phage-bactérie" des souches de *Corynebacterium diphtheriae* type *gravis*, isolées d'un foyer épidémique. [The Peculiarities of "Phage-Bacterium Ecosystems" in the Strains of *Corynebacterium diphtheriae*, *gravis* Type isolated from an Epidemic Focus] Arch. Roumaines Path. Expér. et Microbiol. 1960, Dec., v. 19, No. 4, 485-91, 2 figs. [10 refs.]

In 1959, an epidemic of diphtheria broke out among children living in one region of Rumania, and from 34 patients and 84 contacts *Corynebacterium diphtheriae*

type *gravis* was isolated. One strain, similar in every respect to the others isolated, was studied in greater detail. This strain, like the rest, was toxigenic and it liberated 2 phages spontaneously: phage Pc, which produced clear plaques, and Po ('opaque'), which produced plaques with a dark edge. Bacterial cultures always contained a proportion of cells which were sensitive to the phages produced by the lysogenic, and therefore resistant, cells in the same culture. Phage Po multiplied to much higher titres than Pc, but was more quickly inactivated by heating at 40-54°C. and by various chemical agents. The phages only lysed strains of *C. diphtheriae* isolated from the epidemic focus and from some neighbouring districts and they did not lyse strains sensitive to Freeman's phage B or to phage Varsovie. Antiserum prepared against Po and Pc did not neutralize phages B or Varsovie.

Janice Taverne

MATTHEWS, P. R. J. A Medium for growing Organisms of the Genus *Haemophilus*. J. Med. Lab. Technol. 1960, Oct., v. 17, No. 4, 234-5.

The amount of available V factor in "chocolate" blood-agar has been found to be irregular and this medium is not always satisfactory for the cultivation of *Haemophilus* organisms from pigs. The new medium described consists of a mixture of separately prepared factors X and V components. The X factor comes from a 20% citrated goat's blood (v/v) addition to a basic broth medium, which is heated in a waterbath at 80°C. for 1 hour with intermittent shaking followed by centrifugation. The supernatant is passed through a clarifying filter and autoclaved at 15 lb. for 15 minutes. The V factor medium is prepared by adding baker's yeast 20% w/v to basic broth, heating the mixture, with intermittent shaking, at 80°C. for 1 hour followed by centrifugation. The supernatant is then sterilized by filtration through a Seitz EK pad. The yeast should be fresh and overheating should be avoided.

For the fluid medium equal parts of the 2 broths are mixed and for the solid medium 4 gm. of agar are dissolved in 100 ml. X factor broth at 120°C., which is then allowed to cool to 80°C. before 100 ml. of the V factor broth is added. *Haemophilus influenzae suis* requires 48 hours incubation for optimum growth on the solid medium but other *Haemophilus* strains give good growth after 24 hours incubation.

H. J. Bensted

STRÍZOVÁ, V., VYSTOKÁ-BURIANOVÁ, B. & STÁREK, M., with the technical assistance of M. DRÁBOVÁ & M. CHODĚROVÁ. Studium imunogenních vlastností očkovacích látek proti pertusi. [A Study of the Immunogenic Properties of Pertussis Vaccines] Českoslov. Epidemiol., Mikrobiol., Imunol. Prague. 1960, v. 9, No. 8, 517-22, 3 graphs. [10 refs.] English summary.

A study has been made of the immunizing effect of 4 pertussis vaccines of various types (single, mixed, unadsorbed and adsorbed) manufactured in Czechoslovakia in comparison with the results obtained with 3 vaccines manufactured in Great Britain and Switzerland. Mice

were vaccinated intraperitoneally with various doses of vaccine and challenged by the intracerebral route 14 days later. In the dose required to confer protection against 10^5 organisms the Czech vaccine with 3.5×10^8 organisms per 0.5 ml. lay between the 2 English vaccines (Glaxo and Wellcome), with 2×10^8 and 9×10^8 respectively. In immunized rabbits the rate of production and maximum titres of agglutinins obtained with the Czech vaccines were not inferior to those obtained with the foreign vaccines, and in histamine sensitization tests carried out in mice the Czech vaccines were found to contain less histamine sensitivity factor. *D. J. Bauer*

VAN OYE, E. Liste complète, avec bibliographie, des 163 espèces de *Salmonella* identifiées au Congo et au Ruanda-Urundi. [Complete List and Bibliography of 163 Species of *Salmonella* Isolated in the Congo and Ruanda-Urundi] *Ann. Soc. Belge de Méd. Trop.* 1961, Oct. 31, v. 40, No. 5, 823-36. [10 refs.]

CEFALÙ, M. & FICHERA, G. Der lysogene Zustand der Lysoypen A und D 1 von *S. typhi* und die Umwandlung des Lysoyps A in den Lysoyp D₁. [Lysogenicity of Phage Types A and D₁ of *Salm. typhi* and Transformation of Phage Type A into Phage Type D₁] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 373-9.

The English summary appended to the paper is as follows:—

"1. Only two of the nine subtypes of phage type A could be artificially transformed into phage type D₁ by lysogenization with phage d₁. This fact is an additional proof of the biological heterogeneity of this phage type.

"2. There are two possibilities to obtain phage type D₁: from non-lysogenic Tanarive and from lysogenic Montreal strains.

"A bi-lysogenic phage type D₁ can be produced from the subtype Montreal.

"3. The possibility demonstrated with the subtype Montreal does not occur in nature.

"Examination of naturally occurring strains of phage type D₁ always shows a mono-specific lysogenicity with phage d₁."

CHOMICZEWSKI, J. Untersuchungen über die Beziehungen zwischen den Biochemotypen und Lysoypen von *Salmonella typhi*. [Investigation of the Relations between Biochemical Types and Lysoypes of *Salmonella typhi*] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 380-84. [15 refs.]

The English summary appended to the paper is as follows:—

"The biochemical type and the lysotype of 2002 *Salmonella typhi* strains was determined. Repeated investigations of the strains isolated from certain foci and laboratory experiments disclosed, that the fermentation of arabinosis is a very labile property of the strain,

therefore the biochemotype III should be considered as a variant of the type I and type IV as a variant of the type II. Relations between the biochemical properties and certain lysotypes are confirmed. The ability of strains to form adaptative ferments depends in several cases on the lysotype. The biochemotype II was transformed into Type I by lysogenisation."

CHOMICZEWSKI, J. Ergänzungstypologie der Typhus-Lysotypen F₁ und F₄ mit Hilfe eines neuen Vi-Phagen. [Additional Phage Typing of *Salm. typhi* Phage Types F₁ and F₄ by means of a New Vi Phage] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 388-90.

The English summary appended to the paper is as follows:—

"It is possible to subdivide further the phage types F₁ and F₄ of *S. typhi* by means of the newly isolated phage 'Lodz-13'."

HEYMANN, G. & JANDL, G. Experimentelle Untersuchungen zur Wertbemessung von Typhus-Impfstoffen. II. Mitteilung. Die Wertbemessung nicht extrahierter und nicht adsorbierter Typhus-Impfstoffe nach dem "Allgemeinen Standardprinzip". [Experimental Investigations in connexion with the Standardization of Typhoid Vaccines. II. Standardization of Non-Extracted and Non-Adsorbed Typhoid Vaccines according to the "General Standard Principle"] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Dec., v. 120, No. 5, 367-401, 5 figs. [21 refs.]

The English summary appended to the paper is as follows:—

"1. A series of preliminary tests were performed to obtain an experimental basis for the application of the 'General Standard Principle' to the standardization of typhoid vaccines.

"2. The correlation between the antigenic structure of strains used for the production of the vaccine and the antigenic structure of the infecting strains has previously been studied (1st Communication), using the passive protection test in mice. This correlation could now be confirmed also with the active protection test in mice. Since a vaccine is only able to give protection against any possible infecting strain if it induces antibody production against all antigen fractions of all possible infecting strains, even if such fractions may occur only individually, in standardization procedures the vaccine necessarily must be tested with several antigenetically different typhoid strains.

"3. The strains used for this purpose, Ty-2 (Vi-H-d), Ty-582 (0-9-H-d) and Ty-62 (Vi-), proved to be sufficiently pathogenic in mice, without displaying fatal toxic effects. The mean fatal doses were determined from the infection curves (dose-response-curve).

"4. The intraperitoneal route proved to be the most effective form of immunization.

"5. The production of a typhoid standard vaccine Tyf 1 is described, 273 γ Tyf 1 were defined as protective unit (1 SE).

"6. In a series of active mice protecting tests the linearity of the dose-response-curve of Tyf 1 in the logarithmic probability net (acc. to Hazen) and the parallelism of the straight lines of effect of different vaccines could be demonstrated.

"7. Thereby the prerequisites for the application of the General Standard Principle in the form of the 'three point method' are fulfilled with regard to the standardization of non-extracted and non-adsorbed typhoid vaccines. A model test for the standardization of an unknown vaccine X with the aid of the standard vaccine Tyf 1 is described, and this procedure is recommended for introduction in the standardization technique."

[For Part I, see this *Bulletin*, 1960, v. 35, 924.]

BAKER, E. E. & WHITESIDE, Roberta E. **Vi Antigens of the Enterobacteriaceae. IV. Purification and Properties of Vi Antigen of *S. paratyphi* C.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 328-30, 1 fig. [10 refs.]

In previous papers [this *Bulletin*, 1960, v. 35, 922] the authors have described the isolation and purification of Vi antigen from *Salmonella typhi*, *Escherichia coli* and the ballerup strain 481 and studied their properties. The purified Vi antigens isolated from *Salm. typhi*, *E. coli* and the ballerup strain were found to be serologically identical but there was some suggestion that the Vi antigen prepared from *E. coli* might have immunological properties which were not quite the same as those found in the typhoid and ballerup Vi antigens whose immunizing potencies were about equal.

The mild methods used successfully for the purification of the Vi antigens isolated from *Salm. typhi*, *E. coli* and ballerup were not found suitable for the purification of the antigen obtained from *Salm. paratyphi* C: preparations so obtained examined by the agar-gel precipitation technique disclosed the presence of several antigens other than Vi. Experiments involving the treatment of the crude antigenic extracts with trichloroacetic acid indicated that the contaminating antigens could be eliminated by this procedure. When such preliminary treatment was followed by the methods applied for the purification of the Vi antigens isolated from the other organisms a satisfactory preparation was obtained. Chemical analysis of this *Salm. paratyphi* C Vi antigen gave values which were essentially the same as those obtained with the other Vi preparations. The biological properties were very similar to, if not identical with, those of the Vi antigens obtained from other Enterobacteriaceae.

H. J. Bensted

ANDERSON, E. S. & WILSON, E. Maureen J. Die Bedeutung der *Salmonella typhi murium*-Phagen-Typisierung in der Human- und Veterinärmedizin. [The Importance of *Salmonella typhi-murium* Phage-Typing in Human and Veterinary Medicine] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 368-73.

The English summary appended to the paper is as follows:—

"The revised form of the *S. typhi-murium* phage-typing scheme has enabled us to subdivide this serotype on a finer basis than was hitherto possible.

"The phage-typing of organisms from animal sources on an increased scale has defined characteristic type distributions in particular animals. These distributions can be compared with that in man, and suggestions can thus be made concerning the origins of human infections."

SPANÒ, C. & GULLOTTI, A. **Phage-Typing of *S. typhimurium* in Food-Borne Infections occurring in Various Areas of Italy.** *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 391-4.

"The authors present a survey of phage-typing of 130 *S. typhimurium* strains isolated from various material during 65 food-borne epidemics and sporadic cases in some parts of Italy. The results obtained show that the most frequent type is the 1 a var. 1 widely distributed in this country; the close second set is represented by untypable strains, i.e. strains not lysed by the older phage-preparations of FELIX and CALLOW. The other phage-types encountered in Italy are the following: Type 1 a, 2 a var. 1, Type 2, Type 1, Type 4, Type 1 b and Type 2 c. Strains coming from 9 outbreaks showed lytic patterns different from those reported on the original Schema of FELIX and CALLOW. It may be supposed that they represent further new types of local epidemiological significance."

HUBÁČEK, J. **Phenomic Delay in Transduction of *Salmonella typhimurium* Cell.** [Correspondence.] *Nature.* 1961, Feb. 25, v. 189, 679-80, 1 fig.

In studying the mechanism of transduction of galactose fermentation in *Salmonella typhimurium* with strains *LT₂*(Gal.+) and *SW_{3.51}*(Gal.-) a constitutive galactozymase enzymatic system was found and transduction occurred even in the absence of a specific substrate. It was found, however, that the transduced cells, under these experimental conditions without galactose, multiplied very slowly or not at all. A known number of washed cells of a 48-hour culture of *SW_{3.51}* on complete agar was mixed with the filtrate of the transducing phage (1:1) and exposed for 30 minutes at 37°C. The cell suspension with the adsorbed phage particles was successively diluted and each dilution plated on 2 plates of EMB agar, one with 1% solution of galactose and the other without galactose. The number of colonies fermenting galactose on the EMB+galactose plates indicated the number of inoculated cells with adsorbed phage. The growth from the EMB (without galactose) plates was washed off in saline and the total number of cells and also the number of transduced galactose-fermenting cells was determined. The number of cell divisions in the cultures after 24 or 48 hours' growth, and also the number of cell divisions of the transduced cells were then estimated. It was found that the increased cell division of all cells depended on or was related to the

increased division of the transduced cells and it was therefore concluded that the specific substrate acts only as a selection factor and is not required for transduction. Under the conditions of the experiments—no selection factor and the presence of a large number of recipient cells—there was, however, some inhibition of growth of the transduced cells. The number of divisions of all recipient cells was, on the average, two divisions more than the number of divisions of the transduced cells.

Further experiments to determine whether this delay in the multiplication of the transduced cells was due to changes in the DNA or to the synthesis of new enzymes, by employing chloramphenicol as the inhibitor of the proteosynthesis, were not altogether successful and additional experiments are proposed.

H. J. Bensted

SMITH, D. A. Some Aspects of the Genetics of Methionineless Mutants of *Salmonella typhimurium*. *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 335–53. [Numerous refs.]

BREDE, H. D. *Salmonella stellenbosch*, ein neuer Serotyp (1,9,12:z:1,7). [*Salmonella Stellenbosch, a New Serotype*] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 3, 415–16.

YOUNG, Viola M., GILLEM, Harriette C., MASSEY, E. D. & BAKER, H. J. A Study on the Detection and Specificity of Antibodies to *Shigella flexneri* Types using Preserved Polysaccharide-Sensitized Human Erythrocytes. *Amer. J. Pub. Health.* 1960, Dec., v. 50, No. 12, 1866–72, 4 figs. [14 refs.]

This study was undertaken to determine the applicability of the haemagglutination test, with preserved sensitized human red cells, for the routine serological diagnosis of bacillary dysentery. Comparative tests were undertaken with fresh and preserved cells both of which had been sensitized with Flexner polysaccharide extracts and acute and convalescent-phase sera from patients with Flexner dysentery. The titres found with the two antigens in their respective tests were of the same order and the authors conclude that the preserved antigen, which stored at 4°C. retains its sensitivity and stability for periods up to 6 months, is a satisfactory reagent for use in this diagnostic haemagglutination test and worthy of extensive trial for widespread use as a routine test.

[While there can be no question about the value of the haemagglutination test for serological investigations of certain infectious conditions it is difficult to understand how it could compete as a routine diagnostic technique with the simple straightforward bacteriological cultural methods which offer specific diagnoses in a very high proportion of cases of bacillary dysentery. It is possible that the haemagglutination test could have some value in certain retrospective epidemiological investigations of outbreaks of bacillary dysentery. But this value is strictly limited and Flexner outbreaks would be particularly unsuitable since the ordinary test, like the bacterial agglutination test, cannot differentiate between the various Flexner types owing to the masking by group antibodies.]

In the work reported in this paper there is no indication that any control sera were included in the tests performed. Adequate controls are always necessary in any diagnostic test and in a highly sensitive serological test, such as the haemagglutination test, when the specificity is in doubt it is most essential that a very full series of controls should be examined.]

H. J. Bensted

NICOLLE, P., LE MINOR, L. & LE MINOR, Simone, HAMON, Y. & BRAULT, G., with the technical assistance of Denise DRÉAN & Anne M. DU PLESSIS. La valeur de la lysotypie de quelques sérotypes d'*Escherichia coli* pathogènes pour les nourrissons. Arguments bactériologiques et géographiques. [Value of Phage Typing of Various Serotypes of *Escherichia coli* Pathogenic in Infants. Bacteriological and Geographical Data] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1960, Sept., v. 8, No. 6, 523–62. [14 refs.]

This study is based on the examination of approximately 13,000 cultures of *Escherichia coli*, serotypes O111, O55 and O26, isolated from cases of infant gastro-enteritis in various parts of the world. The phage-typing of the strains belonging to the 3 serotypes was carried out with a set of 28 phages. There appears to have been a good correlation between phage-sensitivity and antigenic structure. For instance with *E. coli* O111 the 11 phages give patterns which were related to the flagellar antigens; those carrying H-antigen 2 gave characteristic patterns with 5 phages in group I, H-antigen 12 with 3 phages in group II and H-antigens 40, 4 and 21 responded to single phages. The authors also utilized the D'Alessandro and Comes reaction in their classification scheme (*Boll. Soc. Ital. Med.*, 1952, v. 31, 291); certain strains of *E. coli* produce a rose-red to brown colour in media containing β -phenylpropionic acid.

The paper contains much detailed information about the geographical distribution and the frequency of the various lysotypes. It is noteworthy that of 282 strains of *E. coli* O55 obtained from various laboratories in Great Britain the majority proved to belong to phage type St. Christopher; this type is associated with H-antigen 2 and is the only type in O55 group which gives a positive D'Alessandro and Comes reaction. Old laboratory cultures tend to lose their sensitivity to phage and a similar difficulty is experienced with strains isolated from patients under antibiotic treatment.

H. J. Bensted

LOVELL, R. & REES, T. A. A Filterable Haemolysin from *Escherichia coli*. [Correspondence.] *Nature.* 1960, Nov. 26, v. 188, 755–6.

This paper reports the production of a filterable thermo-labile haemolysin by *Escherichia coli*, O138, O139, O141 and an unidentified type when these organisms were grown under certain conditions. The culture medium was of first importance. The haemolysin could not be demonstrated in cultures grown in peptone water, ordinary infusion broth or in serum broth with various concentrations of serum, but only in a cooked meat infusion broth medium in which the lean chopped beef had

been first cooked in N/20 aqueous sodium hydroxide before being added to infusion broth. The maximal amount of haemolysin was found in filtrates of cultures grown for 6–10 hours, but it was an unstable product. Heating to 56°C. for 15 minutes destroyed it altogether; after 18 hours at 37°C. its activity was significantly reduced and after 6 days at +4°C. it was found to have lost half its original activity. The haemolysin could be removed from culture-filtrates with 30% ammonium sulphate but when the precipitate was redissolved, dialysed and the isotonicity adjusted much of the haemolytic activity was lost.

These observations are of considerable interest. It will be recalled that BAMFORTH and DUDGEON [this *Bulletin*, 1953, v. 28, 467] considered that the haemolytic activity of *E. coli* was due to the growth of the organism whereas the present authors found that their filterable haemolysin was produced mainly by very young cultures and not by cultures grown for 24 hours or more.

H. J. Bensted

WEIBULL, C. & BECKMAN, H. **Chemical and Metabolic Properties of Various Elements found in Cultures of a Stable *Proteus* L Form.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 379–91, 4 figs. [32 refs.]

COETZEE, J. N. **Lysogenic Conversion in the Genus *Proteus*.** [Correspondence.] *Nature.* 1961, Mar. 18, v. 189, 946–7, 1 fig. [10 refs.]

Bacteria carrying a prophage are normally immune to infection by the homologous phage. Some phages are still able to adsorb but cannot establish themselves in the cell, while other phages fail to adsorb. Of 11 different temperate phages derived from various strains of *Proteus vulgaris* and *P. mirabilis*, 10 failed to adsorb to strains lysogenic with the homologous prophage. When 6 of the bacterial strains were cured of their prophages by UV irradiation, they became sensitive to their respective phages. However, resistant colonies growing up in the plaques were lysogenic and once more failed to adsorb the homologous phage. This inability of the lysogenic cell to adsorb homologous phage is considered to have arisen by lysogenic conversion. Some of the properties of 2 of the phages and their lysogenic cells are reported in more detail. These 2 phages can also cause transduction [COETZEE and SACKS, *Nature*, 1960, v. 185, 869; this *Bulletin*, 1960, v. 35, (702)].

Janice Taverne

SANDYS, G. H. **A New Method of Preventing Swarming of *Proteus* sp. with a Description of a New Medium suitable for Use in Routine Laboratory Practice.** *J. Med. Lab. Technol.* 1960, Oct., v. 17, No. 4, 224–33. [11 refs.]

Many methods have been devised for the inhibition or suppression of swarming in *Proteus* cultures. Swarming is closely associated with the active motility of the organism and the progressive surface-spread of growth from the edge of very young colonies is a characteristic of

most strains of *Proteus* that possess O and H antigens. Natural O variants, such as the OX strains, do not swarm because they are deficient in H antigens and with pure cultures of *Proteus* the development of the H antigens can be suppressed by the inclusion in the culture medium of phenol in a suitable concentration. In mixed cultures or natural specimens containing an unknown flora the disadvantages of employing the usual methods for the suppression of swarming, whether they depend on the narcotic, chemical or mechanical effect of the technique employed, is that they generally have some inhibitory effect on the growth of other organisms which may be present.

The method described in this paper is based on the accidental discovery that *Proteus* strains grown in a medium that was almost entirely deficient in NaCl did not swarm. As a result of this observation a suitable agar medium was evolved which contained only traces of electrolytes and supported growth of organisms commonly found in conjunction with *Proteus* strains and was effective in preventing swarming of the latter. The method has been well tried out as far as *Proteus* strains are concerned and also a number of spreading strains of aerobic spore-bearers: the medium devised compares favourably with other media used for the prevention of swarming and for the support of bacterial growth.

H. J. Bensted

CHIU, V. S. W. & HOEPRICH, P. D. **Susceptibility of *Proteus* and Providence Bacilli to 10 Antibacterial Agents.** *Amer. J. Med. Sci.* 1961, Mar., v. 241, No. 3, 309–21, 5 figs. [23 refs.]

“By means of a carefully standardized tube dilution method, 95 clinical isolates of *Proteus* (representative of the usual United States species distribution) and 12 clinical isolates of Providence group bacilli were tested for susceptibility to 10 anti-infectious agents. Each agent was tested at a number of concentrations. However, the effectiveness of each agent was judged at the test concentration corresponding to the blood concentration attainable in patients.

“Penicillin was the most effective agent against *P. mirabilis*; kanamycin was the most effective agent against *P. rettgeri*, *P. morgani*, *P. vulgaris* and Providence bacilli.”

HUDDLESON, I. F. **Emergence during Growth of *Brucella* Strains on Dye-Agar Media of Cells that show Changes in Sulfur Metabolism.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 1, 91–102, 2 figs. [23 refs.]

Brucella abortus, *Br. melitensis* and *Br. suis* are classified as separate species in accordance with their antigenic structure, growth characteristics on certain dye-agar media, and H₂S production on liver agar slopes. Certain strains of brucellae possess characters which make it difficult to classify them as belonging to a particular species. In addition, cultures of the same strain grown repeatedly on some dye-agar media might show reactions of different intensity, or different colonies of a plate culture may show variations in agglutinability. There

have been suggestions that the differences in the biochemical and serological reactions are merely quantitative and that it might be possible by *in vitro* laboratory procedures to induce changes which would lead to the acquisition by one species of the characteristics of another. This paper is concerned with an attempt by the author to determine whether the biochemical and antigenic characteristics of the three species of *Brucella* could be changed in the laboratory by methods which excluded animal inoculation and, if such changes did occur, whether they were of sufficient degree to substantiate the suggestion indicated above.

Although it was found that bacterial cells of the different species could be adapted to grow on media which previously had inhibited their growth it was not considered that this constituted a mutation. Change in only one enzyme system was demonstrated in certain colonies of the three species—one that decomposes a sulphur-containing compound into H_2S and this is found in most peptones and animal tissue extracts. The other biochemical and antigenic properties of the strains studied failed to show any significant or measurable changes and the results failed to provide confirmatory evidence of the mutation hypothesis. *H. J. Bensted*

LAZUGA, K. & RENOUX, G. Quelques essais sur les bactériophages des *Brucella*. [Experiments with *Brucella* Bacteriophages] *Arch. Inst. Pasteur de Tunis*. 1960, Dec., v. 37, No. 4, 447–52, 2 figs. on pl. [12 refs.]

The sensitivity was determined of 310 strains of *Brucella* to 4 phages which had been isolated from lyso-genic bacteria and from the urine of infected nanny goats. In this way, the *Brucella* strains, which had originated in many different countries, could be divided into 16 groups, although in fact the majority were resistant to all phages. It was noticed that strains falling into 1 of the phage groups had all been isolated in Poland.

In an attempt to relate *Brucella* species and animal source to phage sensitivity, the authors tested a further 63 strains against 19 more phages. At first it appeared that no phages derived from *Br. melitensis* were active on the 4 strains of *Br. suis* tested, but this was later found not to be so. In fact, no species or variety of *Brucella* could be identified by its phage sensitivity, but all phage stocks had been tested undiluted. Tests with critical dilutions of 8 lysates on 5 strains did show specific activity, and the authors are hopeful that a phage typing system for *Brucella* will be practicable.

Janice Taverne

DERTEVA, I. I. The Action of Plague Antiserum on *Pasteurella pestis in vitro* and in Animals. V. The Influence of Plague Antiserum on Changes in the Reactivity of the Body to Plague Antigen. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 3, 499–502. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 797.]

BENNETT, E. O. & WILLIAMS, R. P. Nucleic Acid Phosphorus Content of *Bacillus anthracis* and *Bacillus cereus*. II. The Nucleic Acid Phosphorus Content of the Spores. *Japanese J. Microbiol.* 1960, Apr., v. 4, No. 2, 157–62.

VAN ITERSON, W. Some Features of a Remarkable Organelle in *Bacillus subtilis*. *J. Biophysic. & Biochem. Cytol.* New York. 1961, Jan., v. 9, No. 1, 183–92, 14 figs. [24 refs.]

VAN HEYNINGEN, W. E. & MILLER, Pauline A. The Fixation of Tetanus Toxin by Ganglioside. *J. General Microbiol.* 1961, Jan., v. 24, No. 1, 107–19, 6 figs. [17 refs.]

The combination of tetanus toxin with ganglioside has been investigated by observing the movement of protein peaks in curves obtained with the analytical ultracentrifuge and by electrophoresis for which the Antweiler microelectrophoresis apparatus with schlieren optical attachment was used.

In both methods the movement of the toxin is accelerated in the presence of ganglioside so that the protein toxin peak is largely eliminated and additional peaks appear, corresponding approximately to that obtained with ganglioside alone.

Similar results were not obtained if the ganglioside was replaced by (a) ganglioside free from sialic acid; (b) ganglioside in which the free carboxyl groups of the sialic acid had been methylated by diazomethane; (c) sialic acid alone; (d) ovine mucoid containing sialic acid; and (e) hexosamine-free ganglioside from the red blood corpuscles of the horse.

No evidence could be obtained that the toxin had an enzymic action on the ganglioside.

[See also this *Bulletin*, 1959, v. 34, 944 bis.]

J. W. McLeod

BERNHEIMER, A. W. & VAN HEYNINGEN, W. E. The Relation between the Tetanus Toxin-Fixing and Influenza Virus-Inhibiting Properties of Ganglioside. *J. General Microbiol.* 1961, Jan., v. 24, No. 1, 121–7, 3 figs. [12 refs.]

Previous work by VAN HEYNINGEN and MILLER [see above] has been followed up with observations on the capacity of a variety of ganglioside preparations to inhibit the influenza virus agglutination of chick red blood corpuscles. A table is presented in which the total sialic acid content of different gangliosides, the proportion of this acid liberated by cholera vibrio neuraminidase, the chromatographic characters of these gangliosides, their capacity to react with tetanus toxin and ability to inhibit viral haemagglutination, are compared. This shows considerable correlation between slow movement in chromatographic observations, tetanus toxin fixing capacity and influenza virus agglutination inhibition. The total sialic acid content is related to the tetanus toxin fixing ability but less obviously to the inhibition of virus agglutination.

J. W. McLeod

STERNE, M. & BATTY, Irene. **Toxoiding with Beta-Propiolactone.** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 239-44.

In view of the claim of ORLANS and JONES (*Nature*, 1958, v. 182, 1216) that beta-propiolactone is far superior to formaldehyde for toxoiding *Cl. welchii* toxin type C, the authors have compared the efficiency of formaldehyde and beta-propiolactone in toxoiding *Cl. welchii* type B (lamb dysentery) toxin.

In respect of lack of residual toxicity and persistence of immunizing activities the best formaldehyde toxoid and even those prepared with excess of formaldehyde "over-toxoided" were distinctly superior to beta-propiolactone products. J. W. McLeod

TAKAGI, A., KAWATA, T., YAMAMOTO, S., KUBO, T. & OKITA, S. **Electron Microscopic Studies on Ultrathin Sections of Spores of *Clostridium tetani* and *Clostridium histolyticum*, with special reference to Sporulation and Spore Germination Process.** *Japanese J. Microbiol.* 1960, Apr., v. 4, No. 2, 137-55, 31 figs. [15 refs.]

ERRATUM

It is regretted that the lists of *Leptospira* were transposed in the translated summary of the article by PARNAS, J., KOSLAK, A. and KRUKOWSKA, Maria [this *Bulletin*, 1961, v. 36, 400].

The correct version is as follows:

"(a) Lipase activity was found in the following strains: *L. icterohaemorrhagiae* AB, *L. icterohaemorrhagiae* A, *L. mankarse*, *L. schüffneri*, *L. canicola*, *L. benjamin*, *L. pyrogenes*, *L. australis* B, *L. cynopteri*, *L. sentot*, *L. bangkinang*, *L. autumnalis* A, *L. djasiman*, *L. australis* A, *L. muenchen*, *L. pomona*, *L. grippityphosa* Moscow V and Duyster, *L. hebdomadis*, *L. medanensis*, *L. wolffi*, *L. bataviae*, *L. paidjan*, *L. semarang*."

"(b) No lipase activity was detected in: *L. javanica*, *L. poi*, *L. sarmin*, *L. baiium*, *L. autumnalis* AB, *L. grippityphosa* Bernkopf, *L. hardje*, *L. sejroe*, *L. saxkoebing*, *L. hyos*."

VAN RIEL, J. & VAN RIEL, M. **Analyse antigénique de six souches du séro-groupe *Leptospira hebdomadis*.** [Antigenic Analysis of Six Strains of the *Leptospira hebdomadis* Serogroup] *Ann. Soc. Belge de Méd. Trop.* 1960, June 30, v. 40, No. 3, 549-60. [19 refs.]

The authors report the antigenic characteristics of 6 strains of leptospires isolated from the blood of human patients at Kabunga, Belgian Congo, in 1955-56. All belong to the Hebdomadis serogroup. Cross agglutinin-absorption studies indicate that one strain represents a new sub-serotype of *Leptospira hebdomadis*, for which the designation *L. hebdomadis nona* is proposed. Three other strains (Kambale, Wasaka, and Fungula) appeared

to be closely related to each other but sufficiently different from other known serotypes to justify the proposal of a new serotype, *L. kambale*. The remaining two strains (Tsongo and Kambere Messo) were identified with *L. jules*.

The history of the Hebdomadis serogroup is briefly reviewed, with references. The provisional classification of this serogroup is now as follows:—

Serotype	Sub-serotype	Type Strain
<i>L. hebdomadis</i>	hebdomadis	hebdomadis
	nona	Nona
<i>L. kambale</i>	—	Kambale
<i>L. medanensis</i>	—	Hond HC
<i>L. wolffii</i>	—	3705
<i>L. hardjo</i>	—	Hardjoprajitno
<i>L. sejroe</i>	—	M 84
<i>L. saxkoebing</i>	—	Mus 24
<i>L. kabura</i>	—	Kabura
<i>L. kremastos</i>	—	Kremastos
<i>L. jules</i>	—	Jules
<i>L. mini</i>	sari	Sari
	szwajizak	Szwajizak

L. H. Turner

KARMANSKA, Krystyna. **Badania nad szczepem leptospiiry zwanym szczepem "Tomaszów I".** [Studies on *Leptospira* Strain called "Tomaszów I"] *Med. Dośw. i Mikrob.* Warsaw. 1961, v. 13, No. 1, 19-33, 1 fig.

The English summary appended to the paper is as follows:—

"Taking part in the 1st scientific expedition in Tomaszów Lubelski (organized in 1955 by the Institute of Work and Village Hygiene and by the Department of Research on Leptospirosis I. W.) the author isolated on September 15, 1955 from the blood of a patient afflicted by marsh fever, strain No. 198 later called 'Tomaszów I' strain. As the result of the serological investigations carried out (cross agglutination and cross absorption of antibodies) the author came to the conclusion that 'Tomaszów I' strain probably constitutes a new serotype of *Leptospira*. The isolated strain is slightly virulent for experimental animals; guineapigs and Syrian hamsters did not become ill but the serum antibodies for 'Tomaszów I' strain were found. In 1956 and 1957 the author carried out serological control investigations in the convalescents who were ill in 1955 on the territory of Tomaszów district. Among 41 examined individuals—in 6 reaction was positive (in titres: 1:1000—1:10,000) with 'Tomaszów I' strain. In connection with this the author is of the opinion that 'Tomaszów I' strain played a certain role in the etiology of marsh fever in Lublin district in 1955.

"As a result of later comparative investigations carried out with 'Tomaszów II' strain which was isolated on December 12, 1955 by Durlakowa from the materials of the 1st expedition the author comes to the conclusion that both strains are identical"

VARFOLOMEYEVA, A. A., PEROVA, K. S. & MINIOVICH, F. L. **Effectiveness of Leptospiral Gamma Globulin in Experiments.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 424-31, 2 figs. & 1 diagram. [10 refs.]

In 1914 Japanese workers, experimenting with guinea-pigs, found that serum from human patients convalescing from Weil's disease had protective properties. Convalescent serum was therefore adopted as a specific method of treatment. Later, hyperimmune horse serum was used successfully in Russia; and in 1954 gamma globulins derived from such sera were found to contain large amounts of leptospiral antibodies. The disadvantages of horse serum in the treatment of human beings prompted the authors to investigate the value of bullock hyperimmune serum which was already used for the prevention and treatment of leptospirosis in domestic animals.

Cattle were immunized with an antigen consisting of equal amounts of 3 serotypes of *Leptospira* (*icterohaemorrhagiae*, *grippotyphosa* and *pomona*). Gamma globulin was obtained from the sera of these beasts by fractionation with ethyl alcohol at low temperatures according to a modification of Cohn's method. Agglutination (-lysis) tests showed that the titres of gamma globulin were 2-3 times higher than those of the corresponding hyperimmune sera.

Intramuscular injection of gamma globulin in dosages of 0.1-0.05 [units not stated] protected suckling rabbits (150-300 gm. weight) which were inoculated, after 2 hours, with a lethal dose of a culture of *L. grippotyphosa* and *L. pomona*.

The therapeutic effect of gamma globulin was investigated in suckling rabbits inoculated with virulent *L. grippotyphosa* which, in control animals produced (after 4-5 days) fever, failure to gain weight, and jaundice followed by loss of weight, hypothermia and death after 8-10 days. Gamma globulin was administered to test animals on each of 3 successive days and 2 schedules of doses (ml.) were used: 1-1-1 (total 3 ml.), and 3-1-1 (total 5 ml.). Courses of treatment were started, 4-7 days after inoculation of leptospirae, when the animals were showing signs of illness of varying degrees of severity.

With the 3 ml. schedule, starting on day 4, all of 13 mildly ill (non-icteric) animals recovered.

The 5 ml. schedule, used for the more seriously ill animals all of which were jaundiced, was often started later with the following results: (a) day 4, all of 17 recovered; (b) day 5, all of 8 febrile animals in one experiment, and 4 of 16 (afebrile) in another, recovered; (c) day 6, recovery in 5 out of 7; and (d) day 7, recovery in 4 out of 7. Thus the gamma globulin saved more than 50% of animals which would otherwise have died. The authors conclude that trials of gamma globulin are justified in severely ill domestic animals and human beings; these trials are in progress.

L. H. Turner

MITRA, S. & CHATTERJEE, G. C. **Lecithin-Splitting Enzyme of *Vibrio* El Tor.** [Correspondence.] *Nature*. 1961, Mar. 11, v. 189, 837.

RICKETTSIAE

URBACH, H., SCHABINSKI, M. & LINDE, K. Stoffwechseluntersuchungen an *Rickettsia burneti* im zellfreien Nährsubstrat mit Hilfe der Warburg-Technik und der Bestimmung des assimilierten radioaktiven Phosphors. [Investigations on the Metabolism of *Rickettsia burneti* in Cell-Free Media; O₂ and ³²P Uptake] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 2, 168-79, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 48.]

RIBI, E. & HOYER, B. H. **Purification of Q Fever Rickettsiae by Density-Gradient Sedimentation.** *J. Immunology*. 1960, Sept., v. 85, No. 3, 314-18, 4 figs. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 48.]

ALLISON, A. C. & PERKINS, H. R. **Presence of Cell Walls like those of Bacteria in Rickettsiae.** *Nature*. 1960, Dec. 3, v. 188, 796-8, 1 fig. [17 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 436.]

PICKENS, E. G. & GAON, J. A. **Growth of *Coxiella burnetii* in Agar Tissue Culture.** *Amer. J. Trop. Med. & Hyg.* 1961, Jan., v. 10, No. 1, 49-52, 1 fig.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 792.]

BACTERIOPHAGES

KUBINSKI, H. Serological Studies on the Reaction between Phage T2 and Substances from *Escherichia coli* B Cells. *Bull. Acad. Polonaise des Sci. Warsaw. Sér. Sci. Biol.* 1960, v. 8, No. 12, 559-63, 2 figs. [14 refs.]

Kubinski has reported that incubating T2 phage with an extract obtained by boiling a culture of *Escherichia coli* B made the phage more sensitive to inactivation by potassium permanganate and by formaldehyde, and that after longer incubation the sensitivity decreased [this *Bulletin*, 1961, v. 36, 85, 86]. As the bacterial extract apparently affects the phage tail, and it is the tail which combines with neutralizing antibody, the author has investigated the effect of the extract on phage neutralization.

A T2 lysate was incubated at 37°C. with the *E. coli* extract, and at intervals a sample was withdrawn, mixed with T2 antiserum and the rate of neutralization of the phage in it measured. Mostly, during a period of incubation of up to 90 minutes, the phage was found to be more sensitive to antiserum than untreated phage. However, an increase and decrease in sensitivity occurred, running almost parallel with changes in sensitivity to formaldehyde previously observed. When antiserum against *E. coli* was added to the bacterial-extract-phage mixture, the amount of inactivation of the phage by potassium permanganate was slightly reduced.

The author suggests that before a phage particle actually touches a bacterial cell wall, a substance free in the culture may prime an enzyme in the phage tail, and he draws an analogy with tryptophan which with certain phages, acts as a co-factor in adsorption [*ibid.*, 1959, v. 34, 581.]

Janice Taverner

DAHLGREN, C. M., DECKER, H. M. & HARSTAD, J. B. A Slit Sampler for Collecting T-3 Bacteriophage and Venezuelan Equine Encephalomyelitis Virus. I. Studies with T-3 Bacteriophage. *Applied Microbiol.* Baltimore. 1961, Mar., v. 9, No. 2, 103-5, 1 fig.

KUEHNE, R. W. & GOCHENOUR, W. S., Jr. II. Studies with Venezuelan Equine Encephalomyelitis Virus. *Ibid.*, 106-7.

KESSEL, R. W. I., ARONSON, M. & BRAUN, W. Effects of Brucellaphage on Extracellular and Intracellular *Brucella abortus*. *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 447-50.

In given conditions, 35% of *Brucella abortus* organisms were killed by a *Brucella* phage, as judged by colony formation. The same proportion was killed by phage inactivated by UV but not by phage inactivated by heat. Similar results were obtained when guineapig monocytes containing ingested bacteria were mixed with phage and the bacteria were counted in stained preparations or the monocytes were disrupted and colony counts made.

A protein part of the phage appeared to be concerned in killing part of the bacteria since it was destroyed by heat but not by UV irradiation. It seems likely that it acted in the same way intracellularly as extracellularly and there was some evidence that the whole phage was phagocytosed and not just part of it. It was observed, for instance, that not only did the monocytes contain fewer organisms after mixing with phage but fewer monocytes contained organisms at all.

Janice Taverner

VIRUSES

The order in this section is:—General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.

DUNCAN, I. B. R. Human Thyroid Tissue Culture in Diagnostic Virology. *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 490-500. [15 refs.]

PULVERTAFT *et al.* [this *Bulletin*, 1959, v. 34, 497] described the use of human thyroid cell cultures in diagnostic virology but found them on the whole less satisfactory than other easily available cell types. In this paper the value of thyroid cell cultures in a diagnostic laboratory is described. It was found that the cultures grew very quickly, becoming confluent in 1 or 2 days. They required a change of medium after 24 hours and again when the monolayers were complete. Provided the cells were not used till they were 4 days old toxicity of faecal extracts was not a problem. Cultures could be

maintained for 4-6 weeks in a medium containing 5% calf serum.

The cells proved sensitive (about as sensitive as monkey kidney cells) to all of the prototype enteroviruses (poliomyelitis 1, 2 and 3, Coxsackie B 1-5, Coxsackie A9, ECHO 1-27) except for Coxsackie B 1-5 and ECHO 4, 14, 15, 16, 26 and 27 which did not produce a cytopathic effect. Reovirus type 1 (ECHO 10) also did not cause degeneration of thyroid cells. The thyroid cells were as sensitive as monkey kidney cells for detecting enteroviruses in faeces. The titres of poliomyelitis virus in faeces, especially types 2 and 3, tended to be lower than in monkey kidney cells although sometimes multiplication of these viruses could be demonstrated in normal-looking thyroid cultures by subculture into

monkey kidney cells. On the other hand, titres of most ECHO virus isolates were higher in thyroid cells. The increased sensitivity was most notable for a newly isolated ECHO virus (Frater) which was associated with numerous cases of aseptic meningitis in the Glasgow area in 1959. The thyroid cells were sensitive to the first 17 types of adenovirus (type 12 was not tested). Thyroid cells were much more sensitive to adenovirus in faecal extracts than monkey kidney cells and at least as sensitive to herpes simplex as allantoic membranes of developing chicks. They were also sensitive to vaccinia and cowpox viruses but not to influenza A, B or C, even when haemadsorption was used to detect non-cytopathic virus. Saliva from 5 early cases of measles and vesicle fluid from 1 of chickenpox did not yield a virus when inoculated into human thyroid cells. The 4 groups of cytopathic effects due to the entero-, adeno-, herpes and pox groups of viruses are briefly described.

[This interesting paper clearly brings out the advantages of thyroid cells for diagnostic work. They are easy to obtain and more sensitive to a wider range of viruses than cell types in common use. It is probable (though not discussed by Dr. Duncan) that they are relatively free from the wild viruses which can so easily confuse work with monkey kidney cells.]

A. J. Beale

GIFFORD, G. E. **Manometric Measurement of a Cell-Virus Relationship.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 478-89, 5 figs. [17 refs.]

It was found that HeLa cells infected with poliovirus ceased to take up oxygen (measured in a Warburg apparatus) after about 7 hours when maximal virus was released from the cells. If the multiplicity of infection was low the loss of cells in 1 cycle of multiplication was too small to be detected manometrically. The interpretation that cell killing rather than cell infection was responsible for the low oxygen uptake was confirmed by observing the numbers of dead unattached cells in the Warburg flasks with varying multiplicities of virus infection. From the ratio of the rates of oxygen uptake of normal and infected cells after the first cycle of virus multiplication, the numbers of cells placed in the flask and yield of virus, it was calculated that 1 cell yielded a minimum of 320 plaque-forming units. Antiserum added before or up to 30 minutes after virus effectively prevented cell destruction measurable by this technique but delay of antiserum addition to 60 minutes allowed 60% of the virus to become effective on cells.

A. J. Beale

SCHYMA, D. **Verbesserung der Virusdiagnostik mit Hilfe eines löslichen Ultrafilters. [Improvement of Virus Diagnosis with the Aid of a Soluble Ultrafilter]** *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 1, 17-21, 1 fig.

The author has developed a soluble aluminium lanthanum alginate ultrafilter suitable for the retention of virus particles. The preparation of the membranes follows a previously described method [this *Bulletin*,

1960, v. 35, 1164] with slight modification. 2 volumes of 0.5 M lanthanum nitrate solution are mixed with 1 volume of 0.5 M aluminium chloride solution. A filter paper soaked in the mixture is covered with a layer of 1% sodium alginate solution and then immediately placed in water. The filter thus obtained is then washed, sterilized and stored as described previously. It is 0.4 mm. thick, with a homogeneous zone 60 μ thick and a zone of capillaries 8-9 μ in diameter. 1 sq.cm. of membrane surface passed 1 cc. of water in 35 seconds under a negative pressure of 20 mm.Hg. A membrane 7.5 cm. in diameter can be dissolved in 1 cc. of isotonic sodium citrate solution, and the solution can be directly applied to cell monolayers without any detrimental effect on cell growth.

D. J. Bauer

SCHYMA, D., GÄRTNER, H. & MOLL, G. **Elektronenmikroskopische Darstellung der Feinstruktur eines neuartigen Ultrafilters aus Aluminiumalginat. [Electronmicroscopical Demonstration of the Fine Structure of a New Ultrafilter made of Aluminium alginate]** *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 1, 22-8, 3 figs.

The structure of the soluble aluminium alginate filters developed by Schyma [this *Bulletin*, 1960, v. 35, 1164] has been investigated in the electron microscope. Examination of thin sections showed that the membranes consisted of 3 layers; (1) a homogeneous layer, the primary gel membrane; (2) an intermediate layer, consisting of sharply delimited spongy cavities; (3) a zone of capillaries running at right angles to the surface. Examination of membranes which had been used for filtering off *Escherichia coli* showed that retention of the organisms took place at the boundary between the capillary and intermediate zones.

D. J. Bauer

ISAACS, A., KLEMPERER, H. G. & HITCHCOCK, Griselda. **Studies on the Mechanism of Action of Interferon.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 191-9, 3 figs. [20 refs.]

ISAACS (*Perspectives in Virology*, Vol. 2, 1960, New York, Wiley) proposed 3 hypotheses to account for the action of interferon. The first was that it stimulated glycolysis *per se* increasing the lactate concentration and lowering the pH; the second that by diminishing oxidation of glucose via the pentose cycle it inhibited the production of ribose, needed for the synthesis of virus nucleic acid; and the third that it uncoupled oxidative phosphorylation.

Chick chorioallantoic membranes treated with 2,4-dinitrophenol caused more lactate production and far less interference of MEL influenza virus production than membranes treated with interferon. This suggested that the first hypothesis was incorrect. It was found that influenza virus would grow to high titre in pieces of chorioallantoic membrane suspended in buffered salt solution in which the glucose had been replaced by ribose plus sodium pyruvate; ribose or pyruvate alone yielded very poor virus titres. However, interferon was as effective in the presence of ribose plus pyruvate as in

the presence of glucose, thus demonstrating that the second hypothesis was not correct.

There is evidence that cancer cells produce interferon but are insensitive or weakly sensitive to its antiviral action (Ho and ENDERS, this *Bulletin*, 1960, v. 35, 516; CHANY, C.R. *Acad. Sci.*, 1960, v. 250, 3903). Cancer cells are not dependent on oxidative phosphorylation; if the synthesis of virus required oxidative phosphorylation in normal cells but not in cancer cells, virus synthesis would be inhibited in normal, but not in cancer cells by substances which uncoupled oxidative phosphorylation. Interferon was therefore compared with substances that were known to uncouple oxidative phosphorylation. In experiments with chick membranes, interferon resembled dinitrophenol in uncoupling although the stimulation of glycolysis, the uptake of oxygen and the release of phosphate were less than with dinitrophenol; however, dinitrophenol caused less interference. Sendai virus was 10-fold more sensitive to interferon than Newcastle disease virus (NDV) and was shown to be 3-fold more sensitive to the inhibitory effect of 4 uncoupling agents—dinitrophenol, sodium azide, dicoumarol and Janus green—than NDV.

Interferon does not inhibit the production of more interferon but dinitrophenol was found to inhibit further production. Whereas dinitrophenol inhibits both nuclear and mitochondrial oxidative phosphorylation, dicoumarol and Janus green inhibit only mitochondrial oxidative phosphorylation and yet both substances were found to inhibit virus and interferon production to about the same extent. The authors concluded that interferon production required mitochondrial adenosine triphosphate, and proposed the hypothesis that interferon uncoupled nuclear oxidative phosphorylation and so inhibited virus production but not interferon production. The hypothesis is to be investigated by direct study of oxidative phosphorylation in isolated nuclei and mitochondria.

D. Taylor-Robinson

ŽEMLA, J. & VILCEK, J. **Concentration and Partial Purification of an Interferon.** [Correspondence.] *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 129.

MAYER, V., ŽEMLA, J. & VILCEK, J. **A Method for the Production of an Interferon in Chick-Embryo Cells.** [Correspondence.] *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 130.

OFFICER, J. E. & BROWN, A. **Growth of Psittacosis Virus in Tissue Culture.** *J. Infect. Dis.* 1960, Nov.-Dec., v. 107, No. 3, 283-99, 5 figs. [29 refs.]

This paper reports the results of a study in tissue culture of two strains of psittacosis virus differing in virulence for their natural hosts; 6 BC (parrot strain) and BORG (human strain). They were grown in 2 different tissue culture systems and the points to which attention was principally directed were: rate of infection, rate of multiplication, degree of cytopathic change and morphological development. 2 cell lines were relied on principally: foetal mouse liver and an established line of

human liver (Chang). Though both strains were equally infective for the mouse liver cells, giving 90-100% infectivity, it was the virulent BORG strain only which achieved this rate with human liver, the other strain—6 BC—attaining no more than 2-5%. The virulent strain grew more rapidly and to higher titre and whereas cytopathogenic change was rapid and intense with it, the changes produced by 6 BC were slow in onset and only moderate in degree. It was, however, the difference in the morphological changes exhibited by these 2 strains of psittacosis virus growing intracellularly that was possibly of most interest. With both the first viral forms detectable microscopically were initial bodies, but with the virulent BORG strain further multiplication took place diffusely through the cell cytoplasm, whereas in the case of 6 BC the inclusion grew compactly as a plaque the details of which were indiscernible. Only in the later stages was it possible to see that the plaque had given place to a tightly-packed colony of elementary bodies. The authors express the opinion that multiplication is by binary fission.

S. P. Bedson

MCCLOSKEY, R. V. & MORGAN, H. R. **Latent Viral Infection of Cells in Tissue Culture. VIII. Morphological Observations of Psittacosis Virus in L Cells.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 85-8. [14 refs.]

Studying the latent infection which, as Morgan and his co-workers have shown, can be set up with psittacosis virus in cells deprived of amino-acids and water soluble vitamins, McCloskey and Morgan now show that only some 10% of cells are infected. The remaining 90% resisted repeated exposure to infection, but became susceptible when hydrolysate of yeast extract and phenylalanine were restored to the culture medium. The infection then became overt and spread rapidly throughout the culture so that by the 96th hour almost all cells contained virus. During the latent phase of infection neither by means of the ordinary microscope nor by electron microscopy could any viral structures be seen. Histochemical study of the growing virus confirmed that its inclusions contained both RNA and DNA.

[See also this *Bulletin*, 1956, v. 31, 754, 1270; 1957, v. 32, 1206; 1958, v. 33, 538; 1959, v. 34, 394; 1960, v. 35, 1141.]

S. P. Bedson

BADER, J. P. & MORGAN, H. R. **Latent Viral Infection of Cells in Tissue Culture. IX. Abortive Infection with Psittacosis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1961, Feb., v. 106, No. 2, 311-13, 1 fig.

"L cells which are maintained for 2 or 3 days on phenylalanine- or isoleucine-deficient medium do not support the growth of psittacosis virus and a latent infection is established. Virus can be recovered from these cultures only after addition of a complete medium, but extension beyond 8 days of the interval between infection and addition of complete medium results in a permanent disappearance of infectious virus. Recovered cultures are susceptible to reinfection with psittacosis virus."

TERZIN, A. L., MATUKA, S., FORNAZARIC, M. R. & HLACA, D. M. **Preparation of Group-Specific Bedsonia Antigens for Use in Complement-Fixation Reactions.** *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 78-85.

The title of this paper is a little misleading since it refers to group-specific antigens in the plural, whereas only one has so far been demonstrated in the psittacosis group of infective agents. The work here reported is concerned with the comparison of different preparations of the group antigen. Starting material was infected yolk sac suspension which had been purified to some extent by differential centrifugation. Group antigen was made by boiling and by ether extraction of the boiled material. Both were potent in the complement-fixation test and free from nonspecific and anticomplementary activities; the ether extract was the more potent.

S. P. Bedson

KOVAC, W. Zur Entwicklung und Spezifität der Psittakose im Tierexperiment. I. [On the Development and Specificity of Psittacosis in Animal Experiments. I] *Zent. f. Bakt. I. Abt. Orig.* 1961, v. 181, No. 2, 175-209, 27 figs. [23 refs.]

This paper describes the sequence of histological changes in the development of pneumonia in white mice infected intranasally with psittacosis virus. [Although the author designates these changes and their sequence as "specific", it is difficult to see in what way they merit this qualification. They are, of course, conditioned by the fact that their agent, unlike a bacterium, is a strict intracellular parasite, but there is no evidence here that they are specific for psittacosis.]

S. P. Bedson

JENKIN, H. M., ROSS, M. R. & MOULDER, J. W. **Species-Specific Antigens from the Cell Walls of the Agents of Meningopneumonitis and Feline Pneumonitis.** *J. Immunology*. 1961, Feb., v. 86, No. 2, 123-7. [21 refs.]

Working with 2 viruses of the psittacosis group—meningopneumonitis virus and feline pneumonitis virus—and with antisera prepared against them in the guinea-pig and in the domestic fowl, the authors have studied the distribution and the nature of the antigenic constituents of these two agents. The complement-fixation test and neutralization of infectivity and of toxicity, with and without absorption, were the serological procedures employed; virus in relative purity was obtained from infected allantoic fluid by differential centrifugation.

Extraction of the virus with 1% deoxycholate for 4 hours at 45°C. removed the group-specific antigen, not all of which, however, was destroyed by periodate; there were periodate-resistant as well as periodate-sensitive group antigens. Species-specific activity remained in the deoxycholate-insoluble fraction and was still there after tryptic digestion. Surprisingly the residual species-specific antigen was heat-stable showing no loss of activity after heating at 100°C. for 30 minutes. The trypsin extract had no antigenic activity.

S. P. Bedson

TARIZZO, M. L.; NATAF, R.; DAGHFOUS, T. Études sur le trachome. 1. Isolement et culture en série de 12 souches de virus sur oeuf embryonné. [Studies on Trachoma. I. Isolation and Serial Culture of 12 Strains in Embryonated Eggs] [TARIZZO]. *Bull. World Health Organization*. Geneva. 1961, v. 24, No. 1, 103-5. 2. Action des antibiotiques sur le virus du trachome cultivé dans les oeufs embryonnés. [II. Action of Antibiotics on the Virus Isolated] [TARIZZO, NATAF & DAGHFOUS]. *Ibid.*, 107-13. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 849.]

ENDO, M.; KAMIMURA, T.; AOYAMA, Y.; HAYASHIDA, T.; KINJO, T.; ONO, Y.; KOTERA, S.; SUZUKI, K.; TAJIMA, Y.; ANDO, K.; KUSANO, N.; KAWAI, K. Étude du virus B au Japon. I. Recherche des anticorps neutralisant le virus B chez les singes d'origine japonaise et les singes étrangers importés au Japon. [Study of Virus B in Japan. I. Investigations of Neutralizing Antibodies in Japanese and in Imported Monkeys] [ENDO, KAMIMURA, AOYAMA, HAYASHIDA, KINJO, ONO, KOTERA, SUZUKI, TAJIMA & ANDO]. *Japanese J. Exper. Med.* 1960, June, v. 30, No. 3, 227-33, 4 figs. on pl. [17 refs.] II. Le premier isolement du virus B au Japon [II. First Isolation of Virus B in Japan] [ENDO, KAMIMURA, KUSANO, KAWAI, AOYAMA, TAJIMA, SUZUKI & KOTERA]. *Ibid.*, Oct., No. 5, 385-92, 6 figs. on 2 pls. [12 refs.]

The French summaries may be translated as follows:—

I. During 1958-1959, we have looked for neutralizing antibody against virus B, both in monkeys native to Japan and in imported monkeys.

We have examined a total of 196 specimens of serum from monkeys, of which 44 were positive (22%). The incidence of antibodies among *Macaca fuscata* was 11%, among *M. cyclopis* 16% and among *M. irus* 35%.

II. We have observed a disease characterized by herpetic vesicles in monkeys reared at the Monkey Centre in Japan, and we have isolated a virus and identified it with virus B. Various other authors have isolated virus B from monkeys, either *Macaca mulatta* or *M. irus*, but we isolated it from *M. cyclopis* imported from Formosa.

It is evident from our finding of neutralizing antibodies to virus B [see above], and the present isolation of the virus, that both apparent and inapparent infections exist in indigenous and imported monkeys.

Particular care must therefore be taken to avoid accidental infection of man with virus B, since in Japan poliomyelitis vaccine is beginning to be produced on a large scale and monkeys are now largely used in this work.

However, HULL and NASH [this *Bulletin*, 1960, v. 35, 623] have recently investigated a vaccine against virus B (inactivated by formalin) and MACLEOD, SHIMADA and WALCROFT have also studied active immunization with a formol vaccine, and passive immunization with gamma globulin. Developments of these studies may prevent accidental infection with virus B in man.

ZHDANOV, V. M., DEMIDOVA, S. A. & SVET-MOLDAVSKY, G. J. **Inhibition of Virus and T-Haemagglutination by Typhoid Fever Vi-Antigen.** *Bull. World Health Organization*. Geneva. 1961, v. 24, No. 1, 115-19, 3 figs. [15 refs.]

Erythrocytes were treated with lipo-polysaccharide antigens prepared from *Salmonella typhi* strains possessing Vi antigen. These treated cells were agglutinated to a lower titre by various viruses than were untreated cells. Chick erythrocytes were used with strains of mumps, Sendai virus, influenza A, A1, A2 and B, and guinea-pig cells were used with SE (Stewart-Eddy) polyoma virus. The antigen had no direct action on the virus but reduced the ability of mumps, but not PR8, virus to absorb to red cells. Polyoma virus also absorbed to treated cells as it did to control cells. Red cells treated with RDE were agglutinated by normal horse serum (T agglutination) and this was prevented by treating them with Vi-antigen after the RDE treatment. Horse serum was exhausted of T agglutinin by erythrocytes treated with RDE or RDE + Vi antigen, but not by untreated erythrocytes or those treated with Vi-antigen alone. It was concluded that Vi-antigen "is fixed outside the T-antigen loci" without blocking unmasked T-antigen and in this position "increases the resistance of erythrocytes to agglutination" without destroying the virus receptors.

D. A. J. Tyrrell

CLEELAND, R. & SUGG, J. Y. **Effect of Trypsin on a Susceptible Strain of Influenza A Virus.** *J. Immunology*. 1960, Nov., v. 85, No. 5, 539-45, 2 figs.

Influenza virus A/Se/53 was isolated in 1953 and was maintained as a line (S1) through 167 egg passages. Line S2 was begun in 1956 from the 3rd egg passage of A/Se/53 and had been through 96 egg passages. The haemagglutinating capacity of the S1 line, but not the S2 line or other influenza A strains was completely destroyed (HA titre: 256 to <2) by incubating with 0.25% Difco trypsin for 60 minutes at 37°C. Infectivity for eggs was reduced 99% also. The possibility that the S1 virus during its numerous passages had been replaced by some other virus was disproved since there was a close antigenic relationship between S1 and S2 lines in complement-fixation and neutralization tests.

Crude trypsin inactivated S1 haemagglutinins more rapidly than crystalline trypsin, and other experiments suggested that this was due to the enhancing effect of some other substance in the crude product on its trypsin content. Furthermore, virus infectivity was inactivated most rapidly by crude trypsin although after 24 hours the infectivity titres were approximately the same with either crude or crystalline trypsin. The residual trypsin-resistant infective virus, which was neutralized by immune serum, could not be explained by early inactivation of trypsin since resistant virus still remained after the addition of fresh trypsin. Eggs inoculated with trypsin-treated S1 yielded virus populations composed mainly of trypsin-sensitive virus. However, by repeated subculture with S1 virus treated with trypsin at each passage, subcultures of more resistant virus were obtained; it was therefore necessary to incubate with trypsin for

5 hours and not 1 hour for a significant fall in haemagglutinin and infectivity. Repeated passage of the sensitive virus at either high or low dilution caused no significant change in its susceptibility to trypsin. The authors suggest that this property might provide a marker suitable for genetic studies.

D. Taylor-Robinson

SETO, J. T., NISHI, Y., HICKEY, Betty J. & RASMUSSEN, A. F., Jr. **Relation of Sialidase of Influenza A Viruses to Viral Particles as determined by Electron Microscopy.** *Virology*. New York. 1961, Jan., v. 13, No. 1, 13-18, 4 figs.

5 different strains of influenza A were concentrated and purified by ultracentrifugation. The concentrates were mixed with latex, sprayed and shadowed with uranium in order to count the virus particles present, and the sialidase [neuraminidase] activity was estimated by determining chemically the percentage of sialic acid released under standard conditions. Many particles smaller than typical virus particles were present in preparations of one strain (Japan 305/57) but they were removed by adsorption and elution on red cells and the sialidase activity was unchanged. This strain was the most enzymically active strain. Samples containing 10^8 - 10^9 particles had substantial activity whereas samples of PR8 had similar activity only when they contained 10^{10} - 10^{11} particles.

D. A. J. Tyrrell

KLEMPERER, H. **Glucose Breakdown in Chick Embryo Cells infected with Influenza Virus.** *Virology*. New York. 1961, Jan., v. 13, No. 1, 68-77. [Numerous refs.]

Monolayer cultures of trypsinized chick embryo cells were infected with a large dose of the MEL strain of influenza A. Complement-fixing antigen was first detected after 1.5 hours and haemagglutinin after 2.5 hours. High titres of CF antigen were present by 2.5 hours and of haemagglutinin by 3.5 hours and it was shown that most cells were infected. These cultures were studied biochemically. 30% of glucose uptake was accounted for by aerobic glycolysis but this was almost doubled by 1.5 hours after infection. The direct oxidation of glucose increased by 30-50% at 3 hours after infection. Less than 10% of glucose was oxidized by the pentose pathway and this did not seem to be an important source of ribose in infected or uninfected cells. Methylene blue increased the rate of glucose oxidation in both infected and uninfected cultures to the same level. It was shown that the rate of glucose breakdown in these cultures was limited by phosphate and AMP, for when these were added there was little difference between the rate of breakdown in infected and uninfected cells. It was therefore concluded that the virus produced the observed changes in glucose metabolism by increasing the rate of reoxidation of TPN and the availability of phosphate and of phosphate receptor. [This is a closely written paper with a full discussion and should be read in the original by those interested in the subject.]

D. A. J. Tyrrell

MAYRON, L. W., ROBERT, Barbara, WINZLER, R. J. & RAFELSON, M. E., Jr. **Studies on the Neuraminidase of Influenza Virus. I. Separation and Some Properties of the Enzyme from A Asian and PR8 Strains.** *Arch. Biochemistry*. 1961, Mar., v. 92, No. 3, 475-83, 5 figs. [22 refs.]

LA PLACA, M. & MOSCOVICI, C. I virus parainfluenza. [The Para-Influenza Viruses Group] *Ann. Sclavo*. Siena. 1961, Jan.-Feb., v. 3, No. 1, 63-95, 7 figs. & 1 graph. [74 refs.] English summary (7 lines).

A review.

BELL, S. D., Jr., ROTA, Theresa R. & McCOMB, Dorothy E. **Adenoviruses isolated from Saudi Arabia. III. Six New Serotypes.** *Amer. J. Trop. Med. & Hyg.* 1960, Sept., v. 9, No. 5, 523-6. [10 refs.]

6 new adenovirus serotypes are proposed (19 to 24). The prototypes were found among 65 strains isolated in eastern Saudi Arabia between 1955 and 1957 inclusive [this *Bulletin*, 1960, v. 35, 203]. The prototype strains were isolated from the conjunctivae of children 3 years of age or younger who did not have ocular disease apart from trachoma. The authors were not able to determine whether the agents were the cause of disease in Arabia; strain 931 (proposed type 20) produced conjunctivitis and folliculosis in volunteers [*loc. cit.*]. Each of the new strains possessed complement-fixing antigens common to other adenovirus types but in neutralization tests with rabbit antisera there was no crossing among the 6 prototype strains nor between any of the known 18 serotypes. The prototypes varied greatly in their tissue culture growth characteristics and in their ability to produce specific neutralizing antibody in rabbits. Thus, strain 587 (proposed type 19) rapidly produced complete degeneration in a line of human conjunctival cells and yielded 10^8 TCD50 per ml. but attempts failed to produce antisera with reciprocal titres higher than 32. However, strain 3153 (proposed type 24) with a highest infective titre of $10^{3.7}$ TCD50 per ml. produced a reciprocal neutralizing antibody titre of more than 128. Furthermore, infective titres did not have any relation to haemagglutination titres. In haemagglutination-inhibition tests there was some crossing of the new serotypes, strain 587 was identical to type 10 but was different by neutralization and there was crossing between strains 2711 and 2732 (proposed types 22 and 23) but no crossing in neutralization tests.

Prototype materials were sent to the subcommittee on adenoviruses of the National Institutes of Health. [They have now been officially approved as new types.]

D. Taylor-Robinson

HARUNA, I., YAOI, H., KONO, R. & WATANABE, I. **Separation of Adenovirus by Chromatography on DEAE-Cellulose.** *Virology*. New York. 1961, Feb., v. 13, No. 2, 264-7, 2 figs.

Prototype strains of adenovirus types 1, 3 and 8 were grown in HeLa cells. The infected culture fluids were dialysed against distilled water and then 15-50 ml. amounts loaded on to DEAE-cellulose columns that had been treated with 0.005 M borate buffer at pH 8.1. A continuously increasing concentration of NaCl in borate buffer of the same molarity and pH was then run on to the columns. Adenovirus type 8 was eluted at 0.25 M NaCl, type 3 at 0.3 M NaCl and type 1 between 0.4 M and 0.5 M NaCl. The recovery of infectivity was about 100%, 80% and 60% respectively. Toxin-like material was separated from infective type 1 virus and was eluted at about 0.2 M NaCl. Virus types 1 and 3 were mixed and then separated on a column; each type was eluted at the NaCl concentration characteristic for the type. The evidence for this separation was supported by cross-neutralization tests. The authors discuss the minor differences between their results and those of others [KLEMPERER and PEREIRA, this *Bulletin*, 1960, v. 35, 513; PHILIPSON, *ibid.*, 936] who have worked with adenovirus types 2 and 5.

D. Taylor-Robinson

STANLEY, N. F. **Relationship of Hepatoencephalomyelitis Virus and Reoviruses.** [Correspondence.] *Nature*. 1961, Feb. 25, v. 189, 687.

STANLEY and his colleagues [this *Bulletin*, 1954, v. 29, 120; 1955, v. 30, 451] have described the isolation of a virus, which produces hepatoencephalomyelitis in infant mice, from an Australian aborigine. The virus, except the neurotropic variants whose selection is encouraged by passage of the virus in eggs or tissue culture, causes a characteristic oily skin effect in mice. Stanley now describes work which shows that hepatoencephalomyelitis virus is indistinguishable from the type 3 reovirus described by SABIN [*ibid.*, 1960, v. 35, 514]. Thus, the viruses are indistinguishable in neutralization and haemagglutination-inhibition tests. They share common reovirus group complement-fixing antigens and also agglutinate human group O red cells. Both viruses produce the same clinical and histological lesions in mice.

A. J. Beale

HOSKINS, J. M. **Induction of Cell Competence to Infection by Poliovirus Ribonucleic Acid by Treatment with Molar Sodium Chloride.** *Brit. J. Exper. Path.* 1961, Feb., v. 42, No. 1, 95-8.

It was found that the RNA extracted by cold phenol treatment from type 2 poliovirus (MEF 1 strain) was more active when diluted in M sodium chloride than when diluted in phosphate buffered saline [PBS] with ERK cells as the indicator of infection, but that there was no difference between these two diluents for intact poliovirus or for RNA inoculated intracerebrally into mice. These results suggest that the M sodium chloride acts on the cells rather than stabilizes the nucleic acid. This interpretation was confirmed in experiments in which cells were pre-treated with M sodium chloride for 45 minutes before treatment with virus either in PBS or in M sodium chloride. In these experiments it was found that prior

treatment with M sodium chloride enhanced the sensitivity of the cells to virus diluted in PBS but not to the same level as their sensitivity to virus diluted in M sodium chloride. In this work quantitative assessment of the activity of RNA preparations was marred by the finding that there was not a linear response of ERK cells to dilutions of poliovirus RNA [see also this *Bulletin*, 1959, v. 34, 177].

A. J. Beale

POVALISHINA, T. P. & MIRONOVA, L. L. **Study of the Sensitivity of the Steppe Lemming *Lagurus lagurus* Pall. to Poliomyelitis Virus. I. The Possibility of using the Steppe Lemming in the Study of Poliomyelitis Virus Types II and IV. *Problems of Virology*. London. 1960, v. 5, No. 4, 436-41. [11 refs.] [Translated from Russian.]**

"(1) Sucklings of the steppe lemming have proved highly sensitive to intracerebral infection with types II and IV poliomyelitis viruses (titres of 8 and 7·0 and 7·5 respectively).

"(2) Adult steppe lemmings are susceptible to infection with type II poliomyelitis virus but quite insensitive to type IV.

"(3) In economic terms the steppe lemming is not inferior to white mice and is much more economical and convenient to work with than are cotton rats.

"(4) The steppe lemming can be recommended as a laboratory animal for the study of types II and IV poliomyelitis viruses."

KIRSCHSTEIN, Ruth L., VAN HOOSIER, G. L., Jr. & LI, C. P. **Virus-B Infection of the Central Nervous System of Monkeys used for the Poliomyelitis Vaccine Safety Test. *Amer. J. Path.* 1961, Jan., v. 38, No. 1, 119-25, 5 figs. on pl. [19 refs.]**

26 of 6,300 monkeys used during the safety testing of poliomyelitis vaccine were found to have lesions in the central nervous system [CNS]. In 5 of these animals Virus B was isolated from CNS tissue. 2 monkeys were tested for antibodies to Virus B before and after inoculation of poliomyelitis vaccine and in each case both specimens contained antibodies. All 5 monkeys showed similar CNS lesions which are well illustrated. These changes are severe, particularly around the site of inoculation in the lumbar cord with complete destruction of the normal architecture. The meninges were infiltrated with lymphocytes, and the nerve roots, which showed focal demyelination, with neutrophils. Lesions were less extensive and severe in the thoracic and cervical cords. The pons and medulla were extensively involved with midline lesions involving oedema necrosis and glial infiltration. Lesions were particularly severe on the floor of the 4th ventricle, involving vestibular nuclei, medial longitudinal fasciculi, and nuclei and the spinal tract of the 5th nerve. The lesions were probably the result of lighting

up a latent Virus B infection due to the trauma of the inoculation and the influence of cortisone.

A. J. Beale

VERLINDE, J. D., WILTERDINK, J. B. & MOUTON, R. P. **Presence of Two Interfering Enteroviral Agents (ECHO Virus Type 9 and Poliovirus Type 2) in the Human Central Nervous System. *Arch. f.d. gesamte Virusforschung*. 1961, v. 10, No. 4, 399-407, 1 fig. [14 refs.]**

VERLINDE and WILTERDINK (*Folia Psych. Neurol. et Neurochir. Neerlandica*, 1958, v. 61, 670) described a case of sudden death in an infant from whom an ECHO 9 virus was isolated in suckling mice and monkey kidney cells. This virus caused lesions in the CNS similar to those due to poliovirus but slightly different in distribution [PETTE *et al.*, see below]. This strain was called D 272 and it has now been found to be a mixture of poliovirus type 2 and ECHO 9 with the latter predominating. The mixed virus gave antibodies in rabbits to both viruses. The ECHO 9 was suppressed by growth in a cell line derived from a papilloma of the human bladder allowing recovery of type 2 poliovirus. Single plaque isolation or high dilutions were used to recover ECHO 9. Both viruses sometimes persisted in suckling mice or monkeys. The virus mixtures interfered and mitigated the effects of the single virus. Thus ECHO 9 alone caused more severe disease in mice than the mixture and poliovirus type 2 in monkeys. The exact role of these 2 viruses in the human fatality is unsolved. The case demonstrates the great difficulty of unravelling virus mixtures.

A. J. Beale

PETTE, H., MAASS, G., VALENCIANO, L. & MANNWEILER, K. **Zur Frage der Neuropathogenität von Enteroviren. Experimentelle Untersuchungen zur Neuropathogenität verschiedener Stämme von ECHO-9 Virus. [The Question of the Neuropathogenicity of Enteroviruses. Experimental Investigations on the Neuropathogenicity of Different Strains of ECHO-9 Virus] *Arch. f.d. gesamte Virusforschung*. 1961, v. 10, No. 4, 408-25, 8 figs. [25 refs.]**

The HEV-3, Magdeburg and D 272 strains of ECHO 9 virus were injected intracerebrally and intraspinally into rhesus monkeys, some of which were also treated with cortisone. No signs of illness were observed over a period of 30 days; attempts to isolate the virus from the central nervous system at autopsy were unsuccessful, and no specific lesions could be found in a histological examination of representative areas of the brain and spinal cord. A further group of 3 monkeys was infected similarly with a tissue culture preparation of D 272 virus which was contaminated with type II poliomyelitis virus; 2 animals developed severe paralysis, and histological investigation revealed the presence of lesions typical of poliomyelitis. The dose of poliomyelitis virus used for infection was very small, and it was considered possible that the ECHO 9 strain had acted synergically upon the poliomyelitis infection.

D. J. Bauer

CROWELL, R. L. & SYVERTON, J. T. **The Mammalian Cell-Virus Relationship. VI. Sustained Infection of HeLa Cells by Cocksackie B3 Virus and Effect on Superinfection.** *J. Exper. Med.* 1961, Feb. 1, v. 113, No. 2, 419-35, 9 figs. [23 refs.]

HeLa cells were infected with Cocksackie B3 virus and surviving cells were grown in human serum to form a chronically infected but otherwise normal-appearing population of cells. The sustained infection depended upon the use of human serum which contained Cocksackie B3 antibodies in the growth medium. Only a small proportion of the cells yielded virus. The culture could be cured of Cocksackie B3 infection by prolonged treatment with high titre antiserum. The carrier cultures remained susceptible to poliomyelitis, vaccinia and herpes simplex viruses. The cultures were not susceptible to Cocksackie B1 or B5 virus infection. This was because of surface interference. Cocksackie B1 was adsorbed much less efficiently to carrier cells and the proportion of virus which was adsorbed, like Cocksackie B5 which was also adsorbed, was not eclipsed. RNA from both types of virus produced infection equally well in carrier, cured and parental lines of HeLa cells. The carrier state was thus shown to be due to surface blocking. Interferon, which has been shown to be responsible for some virus carrier states, played no part in this situation [HENLE *et al.*, this *Bulletin*, 1960, v. 35, 200]. A. J. Beale

WENNER, H. A.; LOU, Te-Yong; KAMITSUKA, P. S. **Experimental Infections with Cocksackie Viruses. I. Studies on Virulence and Pathogenesis in *Cynomolgus* Monkeys** [WENNER, LOU & KAMITSUKA]. *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 426-50, 4 figs. [26 refs.] **II. Myocarditis in *Cynomolgus* Monkeys infected with B4 Virus** [LOU, WENNER & KAMITSUKA]. *Ibid.*, 451-64, 10 figs. [27 refs.]

I. This paper presents the results of inoculating 7 strains of Cocksackie virus (Cocksackie A7, B1-6) by several routes into monkeys. The results are summarized in the table.

Cocksackie Viruses in Cynomolgus Monkeys
Number paralysed (including transient weakness and ataxia) over number inoculated

Virus	Dose	Route					Total
		oral	i.m.	intra-	intra-		
				cardiac	spinal		
		1-2 ml.	1 ml.	1 ml.	0-1-0-2 ml		
Coxsackie B1	6.6/ml.	2/3	3/3	1/3	3/3	9/12	
Coxsackie B2	7.0/ml.	0/3	2/3	2/3	2/2	6/11	
Coxsackie B3	6.7/ml.	1/3	0/3	0/3	1/3	2/12	
Coxsackie B4	6.1/ml.	2/3	1/3	1/3	3/3*	7/12	
Coxsackie B5	7.3/ml.	0/3	0/3	1/3	2/3	3/12	
Coxsackie B6	6.4/ml.	0/4	2/4	0/4	4/4	6/16	
Coxsackie A7	5.5/ml.	3/3	2/3	0/3	0/3	5/12	
Total		8/22	10/22	5/22	15/21		

* 1 animal died.

The number of paralysed animals with central nervous [CNS] lesions was 12 out of 17 examined and the authors

conclude that many animals suffered from symptoms due to repeated cisternal puncture. 37 monkeys developed viraemia and 14 had virus in the cerebrospinal fluid [CSF]. All the monkeys tested after virus given intramuscularly or intracardially had neutralizing antibodies of the appropriate type. Myocardial lesions were found in 3 monkeys (B2, B4 and A7), in 1 associated with pericarditis. 1 additional animal had pericarditis (Cocksackie B1). Pancreatitis was seen in 2 animals given B6 virus. 60 monkeys, all of whom failed to produce neutralizing antibodies to polioviruses after the Cocksackie infections, were challenged with virulent type 1 poliovirus orally. No sparing effect was noted by prior infection with Cocksackie B1, 2, 3, 6 and A7 but there was some sparing effect for types B4 and 5. The paralytic rate was about half that experienced by the remaining animals previously infected with other Cocksackie viruses. Moreover, the 2 monkeys which were paralysed as a result of Cocksackie B4 and 5 infection escaped paralysis on challenge with poliovirus.

II. Because of the reported association of Cocksackie B virus and human myocarditis, monkeys were inoculated intravascularly with 10^{7.3} TCD50 of a strain of Cocksackie B4 virus isolated from the myocardium of a fatal human case [KIBRICK and BENIRSCHKE, this *Bulletin*, 1959, v. 34, 319]. 8 monkeys were inoculated intravenously and all survived. 8 attempts were made to inoculate into the left ventricle but only 1 animal survived. 6 monkeys had viraemia on the 2nd day and 2 had virus in the CSF subsequently. Virus was recovered from the heart muscle of 6 out of 7 monkeys killed within 17 days at times when viraemia was no longer present, and from the CNS of 4 monkeys killed between 6 and 10 days.

The lesions seen in the myocardium are illustrated and are similar to those seen in human cases. There were patchy foci with degenerated myofibrils sometimes showing basophilic material in the cytoplasm around or in place of the nucleus surrounded by pleomorphic cellular infiltration. Reparative signs appeared early but may be associated with fresh acute lesions elsewhere in the same heart. Calcification was seen as early as 10 days. The left ventricle bore the brunt of the disease. No electrocardiographic changes were seen during infection. 7 out of the 9 animals had neutralizing substances to Cocksackie B4 virus before infection and most had small rises thereafter. These substances were heat stable (56°C.) but did not prevent infection. A. J. Beale

SPEIR, R. W. **Effect of Several Inorganic Salts on Infectivity of Mengo Virus.** *Proc. Soc. Exper. Biol. & Med.* 1961, Feb., v. 106, No. 2, 402-4. [10 refs.]

BYRNE, R. J. & ROBBINS, Mary L. **Mortality Patterns and Antibody Response in Chicks inoculated with Eastern Equine Encephalomyelitis Virus.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 13-16, 1 fig. [12 refs.]

Subcutaneous inoculation of 9.5 x 10⁷ LD50 of eastern virus (17th mouse passage) into chicks killed all of

10 inoculated at the age of 3 days, 9 of 10 at 4 days, 6 at 5 and 6 days, 3 at 7 days, 5 at 8 days, 1 at 9–11 days and none thereafter. Chicks 14 days old were inoculated and their sera tested for haemagglutinin-inhibiting (HI) and neutralizing (N) antibody. HI antibody (160–640) appeared by the 10th day after inoculation and persisted for at least 140 weeks in all of 3 birds tested for so long. Antibody responses were similar whether the dose was 1 LD₅₀ or 9.5×10^3 LD₅₀. 2 of 5 chicks had HI antibody (640) 5 days after inoculation but none N antibody: 10 days after inoculation all tested had HI (640) and N antibody (indices 35–50): from 20–60 days after inoculation all tested had HI (160–2560) and N antibody (indices ≥ 50).
C. E. Gordon Smith

DANIELS, Joan B., RATNER, Joan J. & BROWN, Sylvia R. **Plaque Reduction, a Sensitive Test for Eastern Encephalitis Antibody.** *Science*. 1961, Mar. 3, v. 133, 640–41.

Sera diluted 1:5 were inactivated and mixed with eastern virus (200 TCD₅₀ per 0.1 ml.). After incubation the mixtures were inoculated on chick embryo cultures in tubes and Petri dishes—the latter were overlaid with agar 1 hour later. Control plates were found to have 25–80 plaques when stained after 72 hours. The presence of virus multiplication in the tubes was detected by haemagglutination of goose cells. In the plates a reduction in plaque count $\geq 80\%$ was regarded as positive for neutralizing antibody, a reduction of 70–79% as equivocal and a lesser reduction as negative.

11 sera from patients $1\frac{1}{2}$ to 22 years after infection were tested. 5 rabbits, 5 crows, 2 blue jays, 4 pigeons, 5 chickens, 5 frogs and 4 squirrels were inoculated with eastern virus and serum samples were taken at intervals. All the animals which had viraemia were found to develop antibody and to maintain it for 9 months. 91 field samples from mammals and birds were also examined.

Of the human sera all were positive by the plaque reduction test but only 5 in the tube test. Altogether 92 of the 229 sera examined were positive by plaque reduction but only 18 in tube tests. None of the inoculated animals which failed to circulate virus had antibody by either test except 1 rabbit. 7 field specimens had antibody by plaque reduction only.

[More information about the distribution of plaque counts in controls and tests is necessary for evaluation of this method.]
C. E. Gordon Smith

ADA, G. L., ANDERSON, S. G. & ABBOT, A. **Purification of Murray Valley Encephalitis Virus.** *J. General Microbiol.* 1961, Feb., v. 24, No. 2, 177–186, 1 fig. on pl.

Murray Valley virus in its 8th mouse passage was propagated in suckling mice. When a brain suspension was treated with protamine there was no significant loss in infectivity and u/v absorption suggested that 80–90% of the associated protein had been eliminated. When protamine-treated material was shaken with fluocarbon there was again no loss of infectivity and a 26–45%

decrease in u/v absorption. Some loss of infectivity occurred on subsequent ammonium sulphate precipitation. After centrifugation at 90,000 g for 30 minutes 90% of the infectivity was in the pellet. The virus could be absorbed on a column of hydroxyl apatite and eluted by a phosphate buffer gradient—maximum elution occurred at 0.1–0.2M. The final purification process used was protamine precipitation followed by absorption and elution from hydroxyl apatite. The 0.1M and 0.2M eluates were then centrifuged at 93,000 g for 12 minutes. Haemagglutinin was recovered at all stages of purification without loss and reached titres of over 10^5 in the final deposit. Haemagglutinin inhibitor was also encountered at all stages but most markedly in the 0.1M and 0.2M fractions. Inhibitor was not found in one experiment made with uninfected brain.

The recovery of infectivity after protamine treatment averaged 70%, in the 0.1M and 0.2M fractions 70% and in the final deposit 15%. The ratio of infectivity to haemagglutinin was 3.4×10^4 in the original material, 1.1×10^4 after protamine, 1.5×10^4 in the 0.1M and 0.2M, and 0.6×10^4 in the final deposit. In the 0.025M column eluate it was over 20×10^4 . Ultra-violet absorptions showed that protein was eliminated by the purification process and that the final deposit was consistently largely RNA. Electron microscopy of this showed large numbers of virus particles without extraneous material. Infective RNA was successfully prepared from the final deposit. The infectivity of the purified virus was much less stable than unpurified although it was fairly stable for at least 1 hour in 10% normal rabbit serum.

C. E. Gordon Smith

MAYER, V. **Plaque Formation by the Tick-Borne Encephalitis Virus.** [Correspondence.] *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 131, 1 fig.

SOKOL, F., ŽEMLA, J., MAYER, V. & LIBÍKOVÁ, H. **Infectious Ribonucleic Acid from Purified Tick-Borne Encephalitis Virus.** [Correspondence.] *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 132.

BLOEDHORN, H. & ACKERMANN, R. Untersuchungen zur Wärmestabilität des Virus der Zentraleuropäischen Encephalitis. [Investigations on the Heat Stability of Central European Encephalitis Virus] *Arch. f.d. gesamte Virusforschung*. 1961, v. 10, No. 4, 522–8, 1 fig. [11 refs.]

The authors have investigated the resistance to thermal inactivation of the Graz I strain of Central European tick-borne encephalitis virus. A 1% suspension of infected mouse brain in 10% horse-serum saline was maintained at 4°C., room temperature and 37°C.; samples were withdrawn at intervals up to 34 days and titrated in mice. No decline in titre was observed after 34 days at 4°C., whereas at room temperature a fall of 2 log units had occurred after 14 days. At 37°C. the virus lost infectivity exponentially with a half-life of 3 hours

J. D. Bauer

MÁLKOVÁ, D., PALA, F. & ŠIDÁK, Z. **Cellular Changes in the White Cell Count, Regional Lymph Node and Spleen during Infection with the Tick-Borne Encephalitis Virus in Mice.** *Acta Virologica*. Prague. 1961, Mar., v. 5, No. 2, 101-11, 4 figs. [14 refs.]

"1. As a result of lethal infection with the tick-borne encephalitis virus in mice a temporary leucopenia appeared in the white blood picture. A significant decrease was recorded in all cellular elements. The intensity of cellular changes was proportional to the intensity of viraemia. As viraemia decreased a reduction took place in the cellular changes (with the exception of eosinophils which disappeared completely).

"2. A significant decrease in lymphocytes appeared in the regional lymph node which corresponded to the persistence of the virus in the lymphatic tissue. The remaining cellular elements in the regional lymph nodes (lymphoblasts, prolymphocytes, as well as macrophages and reticular cells) multiplied.

"3. The changes in the spleen, with the exception of the myeloid component, were irregular and could not be brought into correlation with the virus present in the spleen."

ROIZMAN, B. & SCHLUEDERBERG, Ann E. **Virus Infection of Cells in Mitosis. II. Measles Virus Infection of Mitotic H Ep-2 Cells.** *Proc. Soc. Exper. Biol. & Med.* 1961, Feb., v. 106, No. 2, 320-23, 5 figs.

"Fluorescein labeled antibody staining of HEP-2 cell cultures infected with an inoculum of measles virus free of cell debris and other particulate matter revealed the

presence of measles virus antigen in cells in metaphase, anaphase and telophase. Mitotic cells were shown to be readily recruited into cyncytia induced by measles virus, both in absence and presence of colchicine. These observations contrast with the results of similar studies made in HEP-2 cell cultures infected with Herpes simplex virus and indicate that cells in different stages of the mitotic cycle are not uniformly susceptible to infection with different viruses, or even the same virus."

STERN, H. & FRIEDMANN, I. **Intranuclear Formation of Cytomegalic Inclusion Disease Virus.** [Correspondence.] *Nature*. 1960, Nov. 26, v. 188, 768-70, 3 figs.

A study has been made of the morphology of the Kerr strain of human cytomegalic inclusion disease virus growing in human embryo skin-muscle fibroblast cultures. In electron micrographs of sections of the cells fixed with osmic acid virus material was first observed in the nucleus in the form of masses of granules 80-120 m μ . in diameter with single membranes. Virus particles subsequently passed into the cytoplasm by two methods; (1) singly, the nuclear membrane at the point of exit acquiring extra layers which contributed an outer coat to the particle; (2) groups of virus particles appear to stimulate invagination of the nuclear membrane which forms a vacuole enclosing them; the vacuoles have multiple walls which contribute the outer coat to the virus particles, which may then enter the cytoplasm by extrusion of the whole vacuole from the nucleus or by rupture of the vacuole at the surface of the nucleus. The methods of formation of the virus particle thus resembles that described for herpes virus [this *Bulletin*, 1960, v. 35, 311].

D. J. Bauer

IMMUNITY

BURNET, F. M. **The New Approach to Immunology.** *New England J. of Med.* 1961, Jan. 5, v. 264, No. 1, 24-34. [91 refs.]

This is a concise account not only of the author's own theory of antibody production by clonal selection but also of its application to the mechanism of auto-immune disease in the human being. The sections on self-recognition, the immunologically competent cell, immunologic homeostasis, homograft immunity and graft-versus-host reactions are closely-worded résumés of the work of FAGRAEUS, PAULING, JERNE, WHITE, MEDAWAR and many others, including Burnet himself, and lead on to a discussion on the important impact of this "new" immunology and its intense relevance to the problems of auto-immune disease. This is discussed in relation to three main groups of clinical conditions, viz. (1) conditions due to immunologically based drug reactions such as sedormid purpura; (2) disease due to immune reaction against a normally inaccessible antigen,

for example Hashimoto's disease and idiopathic Addison's disease; and (3) auto-immune disease directed against common body components, such as systemic lupus erythematosus and rheumatoid arthritis. In a succinct conclusion the author admits that selection theories of antibody production and immunity are far from being proved and are constantly being modified. It is however becoming clear that the processes of immunity are essentially a matter of the population dynamics of mesenchymal cells within the body: antibody production is something of only secondary importance.

This is an important paper, listing 91 references, which obviously must be read in the original by all interested in the changing face of immunology. D. A. Cannon

ŠTERZL, J. **Effect of Some Metabolic Inhibitors on Antibody Formation.** [Correspondence.] *Nature*. 1961, Mar. 25, v. 189, 1022-3. [15 refs.]

ODA, M. & PUCK, T. T. **The Interaction of Mammalian Cells with Antibodies. I.** *J. Exper. Med.* 1961, Mar. 1, v. 113, No. 3, 599-610, 1 text fig. & 1 fig. on 2 pls. [12 refs.]

"The single cell plating technique has been applied to quantitation of the reproductive killing of mammalian cells by specific antibodies. This method confirms previous demonstrations by other workers of localization of all the killing activity in the γ -globulin fraction of specific cell antisera but not of normal sera; the need for complement for the killing action in low doses of antibody and the leakage of cell constituents attending cell killing under these conditions. In concentrations of 4 per cent or higher of heated antiserum cell killing occurs without added complement. The cell plating technique permits highly reproducible quantitation of antibody action and demonstrates antibody activity in sera diluted 1:3000. It permits demonstration of very high degrees of species specificity as shown by virtually complete absence of cross-reaction between antisera to Chinese hamster and S3 HeLa cells, respectively. Somatic cells which have been sensitized by absorption of specific antibody lose their sensitization when incubated at 37° unless complement is added within 1 hour."

IPSEN, J. **Changes in Immunity and Antitoxin Level immediately after Secondary Stimulus with Tetanus Toxoid in Rabbits.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 50-55, 1 fig.

The delay in demonstrable antibody response after a secondary stimulus with tetanus toxoid causes concern in the practice of tetanus prophylaxis. As well as measuring circulating antitoxin, the author estimated the total body immunity (before, and at various times from 3 hours to 8 days after, a reinforcing dose of 5 Lf of fluid tetanus toxoid) in rabbits by challenging them with an intramuscular injection of 1,000 lethal rabbit doses of tetanus toxin: prolongation of the survival time is a measurement of increase in immunity, or in the ability of the animal to neutralize toxin, and was shown to start immediately after a second dose of toxoid. The antitoxin level showed no significant rise in the first 2 days after this secondary stimulus. It is inferred that the lag in antitoxin response after a reinforcing dose of tetanus does not reflect a lack of response in terms of total body immunity.

D. A. Cannon

GOWLAND, G. & OAKLEY, C. L. **Acquired Immunological Tolerance of Diphtheria Alum-Precipitated Toxoid in the Domestic Fowl.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 373-8, 4 figs. [15 refs.]

Observations recorded by WOLFE and others [this *Bulletin*, 1958, v. 33, 417, *bis*.] show that injection of protein antigens to chicks in the embryonic stage or soon after hatching results in a depression of antibody production to these antigens if the birds are tested by injection of the same antigen before they are 12 weeks old, but not when the birds are older.

This demonstration of the production of tolerance to antigens by inoculation to the embryo was not successful, however, if the injection was to the yolk sac.

The authors have repeated such observations, using diphtheria APT for injection to the yolk sac and making their challenge inoculation about a year later, injecting diphtheria and tetanus alum-precipitated toxoids intramuscularly to the right and left legs respectively. Samples of blood were withdrawn and tested at intervals of 3 to 4 days from the 6th to the 31st days after challenge. It was found that although the ultimate response was the same in experimental animals and controls there was a delay of about 5 days in the development of antibody to the diphtheria toxoid but not to the tetanus toxoid. They explain the failure of previous observers to elicit this partial evidence of tolerance to the fact that their observations on the antibody content of the sera of their experimental birds were limited to one sample of blood taken on the 9th day, the date at which a maximal response could be expected.

J. W. McLeod

NORTH, E. A. & DOERY, HAZEL M. **Inactivation of Staphylococcal, Tetanus, and Diphtheria Toxins by Ganglioside.** *Brit. J. Exper. Path.* 1961, Feb., v. 42, No. 1, 23-9. [16 refs.]

In the investigation of the effect of injections of sublethal doses of staphylococci to the brain of mice FISHER had observed that osteomyelitis of the skull might follow without any macroscopic evidence of lesion of the nervous tissue (unpublished). This had led the authors to investigate the neutralizing effect of preparations of grey matter on bacterial toxin and in view of BOGOCH's work [this *Bulletin*, 1958, v. 33, 406] and that of VAN HEYNINGEN [*ibid.*, 1959, v. 34, 944 *ter*] the mucolipid ganglioside has been specially investigated. It has been shown that incubation of the staphylococcal and diphtheria toxins for 4 hours with small amounts of ganglioside solutions will neutralize all of these toxins in experiments in which a lethal dose or small multiples of the lethal dose are used and that if the ganglioside solution is heated—optimum 10 minutes at 80°C.—the effect is enhanced for these toxins and also obtained with tetanus toxin. An injection of ganglioside to mice intravenously shortly before challenge with staphylococcus toxin by the same route did not give protection and this may well be related to the observed interference by serum albumin with the protective action of ganglioside. It is suggested that the effect of heating the ganglioside solution may be to liberate sialic acid to which its inhibitory effect on the toxins may be due—a hypothesis under further investigation.

J. W. McLeod

McKINNEY, R. W. & DAVENPORT, F. M. **Studies on the Mechanism of Action of Emulsified Vaccines.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 91-100, 1 fig. [26 refs.]

To test some of the hypotheses of the mode of action whereby oil adjuvant vaccines enhance and prolong antibody production, the authors devised a model system in which mice were injected with emulsified influenza virus

vaccine, the adjuvant being a mixture of Drakeol 6VR and Arlacel A (mannide mono-oleate): serum antibody titrations were performed with the standard method of haemagglutination-inhibition. The rate of breakdown of the emulsified vaccine was studied by injecting emulsions containing 32P, by removal of the granulomata formed at the site of injection (and transplanting them in mice), and by X-irradiation designed to block further antibody production. The results of these interesting experiments cannot easily be summarized and should be studied in the original, but three points emerge: (1) the initial peak level of antibody is dependent upon the virus remaining *in situ* for about 16 days; (2) vaccines emulsified with mineral oil tend to release a large and effective portion

of their antigen soon after inoculation; and (3) the hypothesis that adjuvant vaccine induces the formation of a "local antibody producing organelle" which supplies a major portion of the circulating antibody is inadequate.
D. A. Cannon

RAMON, G. Étude de l'immunité naturellement acquise chez l'homme et chez les animaux: son existence, ses différentes variétés, son mécanisme, ses conséquences. [*Naturally Acquired Immunity in Man and Animals: its Existence, Varieties, Mechanism and Consequences*] *Ann. Sclavo.* Siena. 1961, Jan.-Feb., v. 3, No. 1, 1-36. English summary.

Miscellaneous

HOSPITAL ABSTRACTS. London. 1961, Jan., v. 1, No. 1, 1-68. A Monthly Survey of World Literature prepared by the Ministry of Health.

This is a new publication, prepared by the Ministry of Health and published by HMSO, and is to appear each month. It "aims to cover the whole field of hospitals and their administration, with the exception of strictly medical and related professional matters". It is demy octavo in size, and is clearly printed.

The abstracts are not signed, and most of them are less than about 250 words in length; the original papers to which they refer appeared in many journals—architectural, administrative and medical—and the languages covered include Russian and Scandinavian as well as the other European languages, and, apparently, Japanese.

The broad groups of subjects dealt with include design of hospitals, equipment, staff, administration, finance, supplies, catering, laundries, hygiene, accidents, services for the patients, special departments and units, and special hospitals. There are many subdivisions and there is an author index. The publication should be very useful.
Charles Wilcocks

LARSON, P. S., HAAG, H. B. & SILVETTE, H. *Changing Concepts of the Role of Tobacco in the Management of Disease.* *Amer. J. Med. Sci.* 1960, Nov., v. 240, No. 5, 613-35. [246 refs.]

This is a well documented review of the attitudes towards tobacco in the presence of disease. The tenor of the article is well summarized by the concluding phrase "the categorical imperative must sometimes yield to individual considerations". The subjects covered include tobacco allergy, tobacco angina, tobacco amblyopia, cardiovascular disease, hypertension, angina pectoris, myocardial infarctions, peripheral vascular disease, pulmonary emphysema and tuberculosis and peptic ulcer. Little, if any, mention is made of the role of tobacco in the aetiology of these and other diseases, but summaries are given of the evidence of harmful effects when patients with the above diseases smoke. The authors condemn all forms of tobacco in tobacco allergy, angina and amblyopia, but point out that in established cardiovascular diseases (excluding thromboangiitis obliterans) a moderate amount of smoking may do no harm. Most authorities agree that smoking is harmful for patients with emphysema and pulmonary tuberculosis; the statements as regards peptic ulceration are more varied.

W. W. Holland

Book Reviews

JOHNSTONE, Rutherford T. [M.D.] & MILLER, Seward E. [M.D.] *Occupational Diseases and Industrial Medicine.* pp. vii + 482, illustrated. 1960. Philadelphia. London: W. B. Saunders Co.

This textbook is intended for students and teachers of occupational medicine and also for practitioners faced with problems arising out of industrial conditions.

Part I of the book covers the elements of industrial medicine. Wise employers have found it good business to provide in-plant occupational medical services designed to place workers in jobs most suited to them, and to keep them in good health and fit for their work. How this is to be achieved is described in the first 83 pages and although some of the advice is applicable only in America, the industrial physician elsewhere may find

useful information. Emphasis is placed on the preventive or health conservation aspect and in particular on keeping detailed records of examinations. Well-kept records may help in detecting a possible cancer risk in a works group, and in the early recognition and therapy of mental illness.

In discussing Workmen's Compensation the authors express strong views on attempts made to amend the Compensation Acts so that they become matters of health or social insurance. This complaint reminds one of the difficulty sometimes met with in Great Britain of keeping the scope of the National Insurance (Industrial Injuries) Act separate from that of the National Health Act. Employer liability in the United States obstructs the placement in suitable jobs of workers suffering from non-industrial disease. The employment of the handicapped would be good business but courts have been awarding large settlements for cardiac deaths and cardio-vascular accidents. Employers are therefore reluctant to employ persons with chronic degenerative disease.

In the final chapter of Part I, the Diagnosis of Occupational Disease, which serves as an introduction to Part II, the use of the epidemiological approach is advocated.

Part II, on Occupational Diseases, shows signs of the times in that metals such as lead which at one time played a prominent part in industrial medicine are relegated to a later chapter of their own. The advances of chemistry in modern times have added greatly to the number of toxic materials. The hydrocarbons constitute the largest group of chemicals met with in industry, and the number of their combinations is infinite. This reviewer well remembers his appreciation, as a student, of the fact that the professor of physiology took half an hour of lecture time to discuss the elements of organic chemistry so as to explain the constitution of the protein molecule. The authors preface Part II with a review of the basic principles of organic chemistry, which will be equally valuable to students.

The industrial uses and effects of all the major toxic chemicals and noxious agents are set out in paragraphs headed occupational exposure, pathology, signs and symptoms, treatment, disability both transient and permanent, prevention and so on. Where particular sites or organs are specially affected, these are discussed separately and where special laboratory or other tests are in use these are given in full. An excellent feature is the case histories given at the end of the description of many of the diseases. These bring out vividly the types of exposure and the effects and in some cases show the necessity of a careful differential diagnosis. Threshold limits (maximum allowable concentrations: MAC) are not mentioned particularly in the text but there is an Appendix which gives lists of the values recommended by the American Conference of Governmental Hygienists in 1959 and by a Committee of the same body in 1960 [*Arch. Indust. Health*, Chicago, 1959, v. 20, 266; this *Bulletin*, 1960, v. 35 (26)].

Noxious gases, aliphatic, halogenated and aromatic hydrocarbons are the first toxic agents to be considered and this is done faithfully in 4 chapters. Then a chapter is devoted to the pneumoconioses which are classified into major, minor and benign types. The effects of

vegetable dusts are placed among the minor pneumoconioses: it might have been better to keep these separately. However the aetiology, pathology, signs and effects of all forms of dust disease are fully detailed. It is to be regretted that no mention is made of the Caplan-Colinet syndrome in which pneumoconiosis is modified in the presence of rheumatoid arthritis. The attitude of the authors to pulmonary function tests may be summed up in their own words. "Although these pulmonary function tests estimate disability with considerable accuracy, they are rarely of value in establishing the etiology of the disability. There is no intent here to decry their use, but we do not believe that they are the complete answer to the problem of estimating disability even though this belief may be held by a few chest specialists and compensation boards."

Under Metals and Metalloids the toxic effects of some 38 elements and their compounds are described, not in order of importance but in alphabetical order. Some are not of great importance. As might have been expected, since berylliosis was first fully investigated in the United States, there is an excellent short account of the condition, completed by an illuminating case history. In cadmium poisoning acute intoxication affects the lungs; pathological findings in other organs are minimal and not the primary cause of death. In a short review of the diverse opinions on chronic exposures BONNELL *et al.* [this *Bulletin*, 1959, v. 34, 1025] are quoted "Chronic cadmium poisoning is an insidious disease associated with the development of emphysema and renal damage". The authors state that they have not seen a case of chronic poisoning and give PRINCE'S opinion [*ibid.*, 1948, v. 23, 40] that in chronic exposures there is probably a rapid elimination of cadmium and there is no cumulative effect.

Occupational cancers are divided into those where the cause is an established carcinogen and those where the cause is doubtfully industrial. Asbestos is placed in this second group; it probably acts as a cocarcinogen, that is a substance which hastens the action and increases the potency of carcinogens. Cancer is most difficult to establish as occupational in origin. Therefore the epidemiological approach is the best and this, as stated before, may depend on good industrial records. A chapter is devoted to propellants, fuels and oxidizers. Surrounding the rocket missile programme in the United States there is considerable secrecy but in fact most of the chemicals found in propellants are common to other industries. There are exceptions such as the boron hydrides and the derivatives of hydrazine, and particulars of the effects of these are given. As the industry is rapidly developing, the chapter is presented as a progress report.

We are told that "there is probably no other chemical which receives such rigid study on its hazards to various forms of life before it is marketed than does a new pesticide". This rigid legal control in the United States arose from the necessity to protect not only the worker engaged in the manufacture of the pesticide but also the farmer who uses it and those within the home who may handle it or eat contaminated food.

The two final chapters cover the physical agents from vibration disease to changes produced by electromagnetic energy such as infra-red radiations. The last chapter is

designed for the individual who possesses little previous knowledge of the subject of ionizing radiations. Nevertheless it provides a useful review of the present risks.

A glossary of industrial terms completes a textbook which certainly fulfils the object of the authors to provide a book for those entering the field of industrial medicine. We find that it reflects the opinions and attitude of the experts in the United States. In this and other ways the book will be useful to other experts.

Charles L. Sutherland

MINISTRY OF HEALTH: DEPT. OF HEALTH FOR SCOTLAND.
Radiological Hazards to Patients. Second Report of the Committee.

This book was reviewed on p. 342.

TURNER, C. E. [A.M., Ed.M., D.Sc., Dr.P.H.], SEL-
LERY, C. Morley [A.B., M.D.] & SMITH, Sara Louise
[M.A. Ed.D.]. **School Health and Health Educa-
tion. With special consideration of the
Teacher's Part in the School Health Program.**
4th Edition. 481 pp., 35 figs. 1961. St. Louis:
The C. V. Mosby Co., London: Henry Kimpton,
134, Great Portland Street, W.1. [37s. 6d.]

There is an obvious need to enlist the cooperation of the teachers if any school health service is to be satisfactory. As the causes of illness and disability in the school population change from the complications of the infectious diseases and the major disabilities resulting from rheumatic heart disease, rickets, and non-respiratory tuberculosis, to behaviour problems, problems of mental health and minor deviations from an expected high physical standard, so the cooperation of the teacher becomes more and more necessary. This book discusses in detail many aspects of the work of the school health services and the opportunities for health education in schools. Such education in schools is particularly important because the children are at a period of habit formation, and because it reaches, through the schools, the whole generation of children and hence the adults of the future.

The information given in this book is reliable and up-to-date. There are chapters describing the various members of the school health team, the characteristics and normal variations of healthy children, some common defects and diseases, the common communicable diseases, the need for a healthy school environment and the role of the routine medical examination in early diagnosis and the promotion of health. Later chapters describe methods of teaching health, and the book concludes with an interesting chapter on evaluation. It is suggested this can be done partly by evaluating the administrative details of health education activities such as the amount of time and effort put into health education in the school, as well as by measuring the effect on the children. Ways of doing this include the direct observation of the children by the school staff to see if their habits have, in fact,

changed, the use of questionnaires completed by the children and their parents, individual observation of children and conversations with the parents, by a follow-up examination of health records, and by detailed case studies of individuals. *M. D. Warren*

CLARK, Paul F. **Pioneer Microbiologists of America.**
pp. xiv + 369, illustrated, 1961. Madison 6: The
University of Wisconsin Press, 430 Sterling Court,
Wisconsin. [\$6.00.]

Microbiology, as an organized science, is only about 100 years old, although it is almost 300 years since Antonius van LEEUWENHOEK wrote the first of his remarkable series of letters to OLDENBURG, the Secretary of the Royal Society, in which he described bacteria and other forms of microscopic life previously quite unknown or even imagined. It was during the latter half of the 19th century that the intense study of micro-organisms by European scientists, mainly French and German, led to the very rapid development of our knowledge in this field. The achievements of the French and German workers completely overshadowed the few fundamental discoveries made by the small number of English scientists who were interested in the study of bacteria at that time. America was almost entirely dependent on the achievements of European workers for their understanding of infectious diseases.

The author of this book, Dr. Clark, is Emeritus Professor of Medical Microbiology in the University of Wisconsin. He was appointed as head of that department during the First World War and came from the Rockefeller Institute where he was one of FLEXNER's assistants. He was therefore in a position to watch the development of microbiology both in the schools and universities and also the research institutes. In addition he knew personally most of the earliest workers in the country and is thus able to assess their personal values, which is not possible for those who are familiar only with their scientific writings.

The introductory chapters describe the early development of the science in other countries, the work of JENNER, the achievements of John SNOW and William BUDD, PASTEUR, LISTER, KOCH and others. The great American story of yellow fever, of course, has its place but it is modestly told and is reasonably just to Carlos FINLAY. At the outset the author set his pioneer period from the Victorian era until the First World War, only extending the period when a particular story requires it. The yellow fever story extends to 1928 to include the tragic personality of NOGUCHI. If the story of BRILL's disease could also have been extended the great achievement of Hans ZINSSER could have been recorded. But there must be limitations. The work of some of the pioneers precedes that of others, but very roughly they belong to the same period and they are more or less classified in accordance with the geographical position of the institution with which they were long associated. The author begins with Johns Hopkins University and passes on to the other universities and institutes in the Eastern Seaboard States and proceeds westward picking up the pioneers one by one

until he reaches the Californian coast. It is not a continuous story of microbiology; it is often discontinuous but generally as a name comes up it is associated with some scientific contribution or the part played by the man in the early development of microbiology or preventive medicine or there may be a pen-portrait of the man himself. There are a great many names in the total list, for in addition to medical bacteriologists, there are veterinary and plant pathologists; there are others whose achievements have not been strictly microbiological. Well over 100 receive a major mention and many more a brief reference. There are the outstanding personalities among the pioneers such as William WELCH, Theobald SMITH, Simon FLEXNER, W. H. PARK and others like Walter REED and RICKETTS who get considerable space. There can be no doubt that Theobald Smith can be regarded internationally as one of the greatest masters of bacteriology but Welch's claim to eminence did not rest only on his technical achievements in microbiology. He was a great man and a leader of others; the greatest giant of all the giants at Johns Hopkins. Welch by his own personality attracted so much talent that his department became pre-eminent among the American universities and most of those who worked with him moved on to occupy chairs themselves or directorships of research institutes, MACCALLUM, COUNCILMAN, FLEXNER and our own NUTTALL about whom the author speaks very graciously.

Dr. Clark has spread his net widely and there can be few early American bacteriologists with any claim to be remembered whom he has not included in his list and told something of their work. There are, however, some omissions; MUSGRAVE and DUVAL for instance. About the turn of the century both made valuable con-

tributions to the bacteriology of bacillary dysentery. Duval, especially, deserves to be remembered for he independently of KRUSE, described the organism later to be known as *Shigelli sonnei*; in America it was often called the Sonne-Duval bacillus. The author may not be particularly interested in the early history of the dysentery of the dysentery bacilli for he has rather confused the issue over the cultures Flexner collected in the Philippines in 1900. There is some excuse for this as there was very considerable confusion at the time. Nevertheless Flexner did find Shiga dysentery in the islands but only one of the cultures he brought back was found, at the subsequent examination by MARTINI and LENTZ, to be indistinguishable from Shiga's bacillus; the others had the characters of the group designated by Kruse as para-dysentery organisms. But these are not very serious slips.

It is difficult to judge the book as a history of microbiology in America in the early years and it is doubtful if the author's intention was more than to write an account of the men and women in the universities, colleges and institutes of America who had either made direct contributions to the advancement of microbiological knowledge or indirectly by organized academic teaching and other methods for the adequate equipping of future generations of workers in this field. There is a reasonably good index, but the planning of the book and the method of documentation make it less suitable for reference than it could have been. There is an excellent series of photographs of a number of the pioneer workers and the book makes interesting reading especially to those who, like the reviewer, belong to a generation not far removed from that of the pioneers themselves and who can remember so many of them and their work.

H. J. Bensted

We record with deep regret the death on 23rd April, 1961 of Claude Lillingston, B.A., M.D., who had been a contributor to this *Bulletin* from 1932 to 1961.